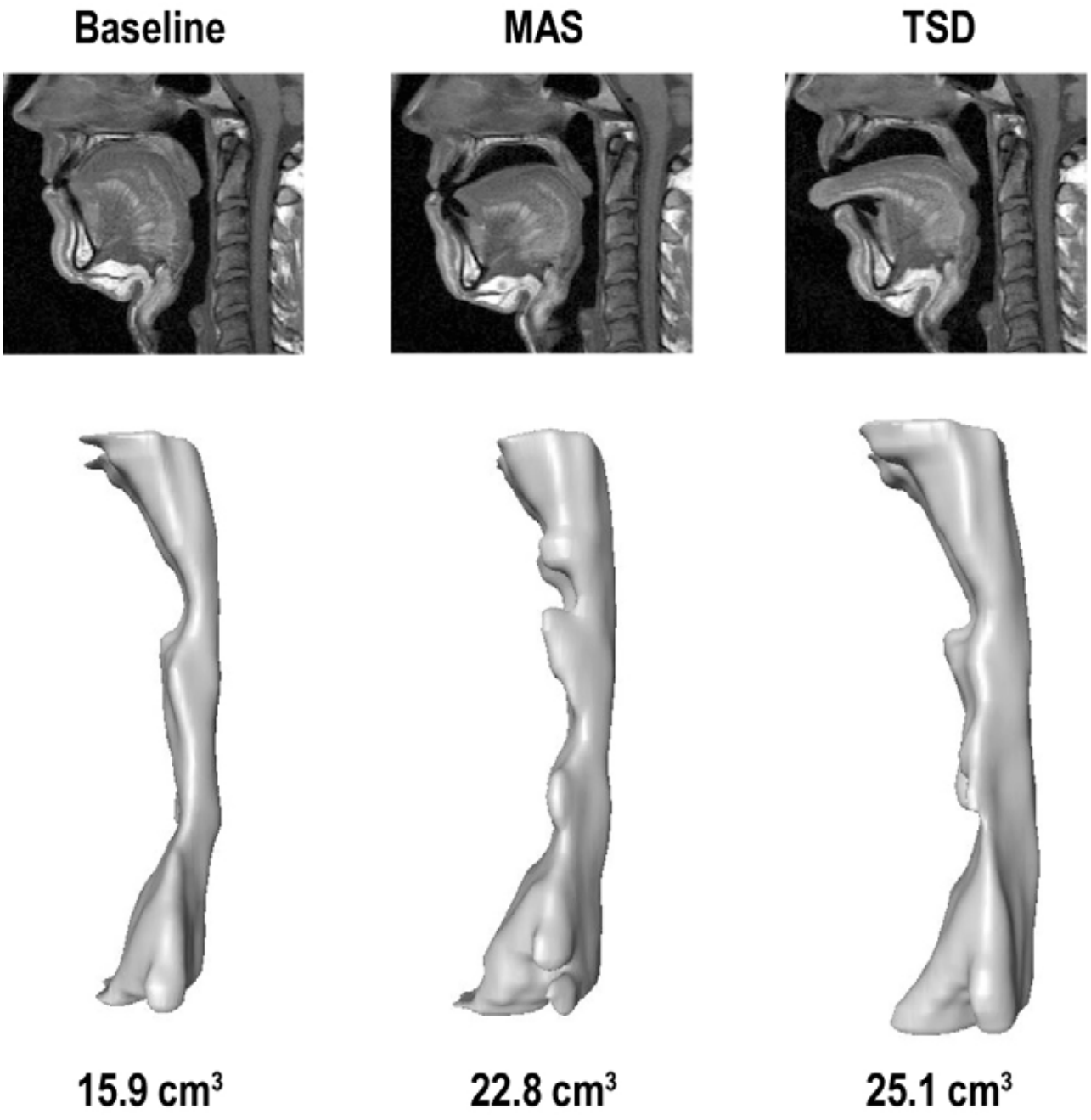
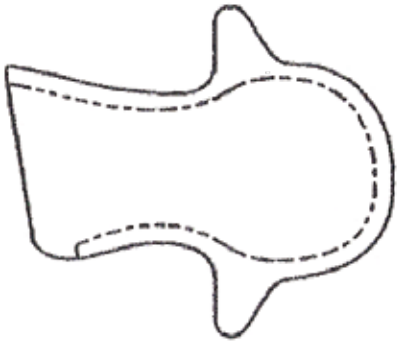
aveoTSD®

Clinical Papers

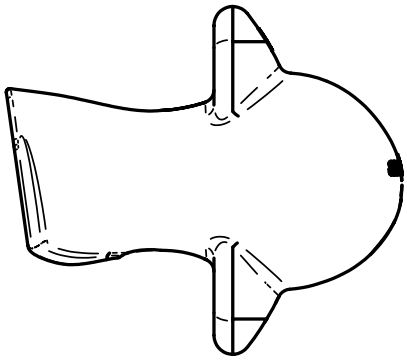


MRI's courtesy of Upper Airway Effects of Two Oral Appliances—Sutherland et al

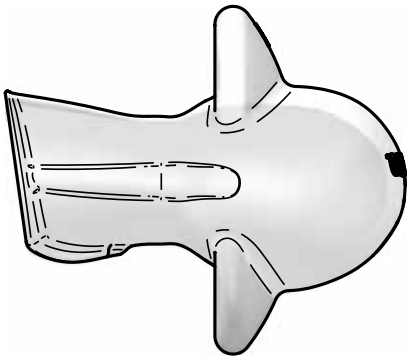
Development
aveoTSD® Design



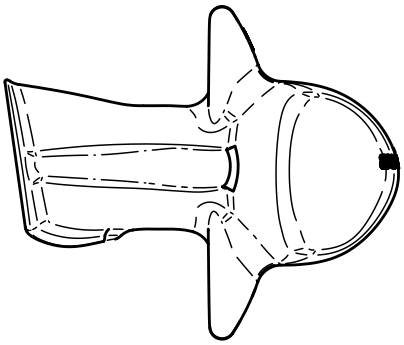
MK 2 2005
First molded TSD
2.6mm silicone wall thickness
PLEASE NOTE: This version of the aveoTSD was used for **ALL** published clinical papers to date.
The following design aveoTSD methodically addressed clinical studies compliance objections, with refinement by user feedback.



MK 3 2007
1.1mm silicone wall thickness
Extended V notch
V notch bumper



MK 4 2009
0.4mm silicone wall thickness
Lateral spar
Increased lip tab
Contoured lip tab
4mm wide isthmus
Reduced bulb ceiling



MK 5 2010
Reduced bulb volume
Reduced tab thickness
Reduced tab height
Increased isthmus
Softer material
3 sizes
Current design in production

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The Efficacy of a Novel Tongue-Stabilizing Device on Polysomnographic Variables in Sleep-Disordered Breathing: A Pilot Study

Ruth N. Kingshott, Ph.D.,1 David R. Jones, R.P.S.G.T.,1 D. Robin Taylor, M.D.,1 and Christopher J. Robertson, M.D.S. 2

1 Respiratory Research Unit, Dunedin School of Medicine and 2 Department of Oral Sciences & Orthodontics, University of Otago, Dunedin, New Zealand.

Sleep And Breathing, Vol. 6, Number 2, 2002

Tongue Related Papers

Return of the TRD

Commentary on Lazard D, et al. The tongue-retaining device: Efficacy and side effects in obstructive sleep apnea. J Clin Sleep Med 2009;5:431-438.

Rosalind Cartwright, Ph.D.

Rush University Medical Center, Chicago, IL

Journal of Clinical Sleep Medicine, Vol.5, No. 5, 2009

The Origin of Pharyngeal Obstruction during Sleep

Laurence I. Barsh, M.M.D.

Sleep And Breathing, Vol. 3, Number 1, 1999

The Great Leap Forward: the anatomic basis for the acquisition of speech and obstructive sleep apnea

Terence M. Davidson

Department of Otolaryngology – Head and Neck Surgery, University of California, San Diego and the VA San Diego Health Care System, San Diego, CA, USA

Sleep Medicine 4 (2003) 185–194

Comparative Effects of Two Oral Appliances on Upper Airway Structure in Obstructive Sleep Apnea

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Study Objectives: Oral appliances are increasingly being used for treatment of obstructive sleep apnea (OSA). Mandibular advancement splint (MAS) mechanically protrudes the mandible, while the tongue stabilizing device (TSD) protrudes and holds the tongue using suction. Although both appliances can significantly improve or ameliorate OSA, their comparative effects on upper airway structure have not been investigated.

Design: Cohort study.

Setting: Sleep Investigation Unit.

Patients: 39 patients undergoing oral appliance treatment for OSA.

Interventions: OSA patients underwent magnetic resonance imaging (MRI) of the upper airway during wakefulness at baseline and with MAS and TSD in randomized order. Treatment efficacy was determined by polysomnography in a subset of 18 patients.

Measurements and Results: Upper airway lumen and surrounding soft tissue structures were segmented using image analysis software. Upper airway dimensions and soft tissue centroid movements were determined. Both appliances altered upper airway geometry, associated with movement of the parapharyngeal fat pads away from the airway. TSD increased velopharyngeal lateral diameter to a greater extent (+0.35 ± 0.07 *vs.* +0.18 ± 0.05 cm; P < 0.001) and also increased antero-posterior diameter with anterior displacement of the tongue (0.68 ± 0.04 cm; P < 0.001) and soft palate (0.12 ± 0.03 cm; P < 0.001). MAS resulted in significant anterior displacement of the tongue base muscles (0.35 ± 0.04 cm). TSD responders (AHI reduction ≥ 50%) increased velopharyngeal volume more than non-responders (+2.65 ± 0.9 vs. –0.44 ± 0.8 cm^3; P < 0.05). Airway structures did not differ between MAS responders and non-responders.

Conclusions: These results indicate that the patterns and magnitude of changes in upper airway structure differ between appliances. Further studies are warranted to evaluate the clinical relevance of these changes, and whether they can be used to predict treatment outcome.

Keywords: Magnetic resonance imaging, mandibular advancement splints, obstructive sleep apnoea, tongue stabilising device, upper airway

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INTRODUCTION

Oral appliances offer an effective alternative to continuous positive airway pressure (CPAP) in the treatment of obstructive sleep apnea (OSA).[1] Oral appliances can be categorized into two design types; the mandibular advancement splint (MAS) and the tongue stabilizing device (TSD). MAS devices attach to the dental arches and mechanically protrude the mandible, whereas TSDs consist of a preformed bulb, which holds and protrudes the tongue using suction.

MAS are the most common type of oral appliance, and mounting evidence supports their use for the treatment of OSA.[2] The clinical practice parameters of the American Academy of Sleep Medicine currently recommend the use of MAS for the treatment of mild to moderate OSA, and for severe OSA when patients refuse or are unable to tolerate CPAP.[3]

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TSD are used less commonly, and investigations into their efficacy remain limited.[4-8] Tongue protrusion using these devices has been shown to lead to improvements in OSA, with demonstrated reductions in AHI, arousal frequency, and oxygen desaturation,[4,6-8] as well as improvement in daytime sleepiness.[6,9] TSD has been proposed as a treatment option for patients with dental contraindications (hypodontia, edentulism, periodontal disease), which preclude the use of MAS.

The aim of oral appliance therapy is to improve upper airway patency, thereby preventing pharyngeal collapse during sleep. Various imaging techniques have demonstrated increased upper airway dimensions with mandible or tongue protrusion.[2,10-12] However, understanding of the exact mechanisms by which oral appliances improve OSA remains limited. Magnetic resonance imaging (MRI) is the modality of choice for 3-dimensional analyses of the upper airway and surrounding soft tissue structures.[13,14] We have recently used MRI in the largest and most detailed assessment to date of the effects of MAS on upper airway structure.[15] However, there are few studies examining the effects of TSD on upper airway structure and no data about the commercially available TSD.

The different modes of action of these appliances (mandible versus tongue protrusion) are likely to differentially influence upper airway caliber and shape and surrounding soft tissues. There have been no direct comparisons of the anatomical effects of these oral appliances. Assessment of upper airway

structures with MAS and TSD could provide insights into their respective sites and mechanisms of action. This study aimed to assess and compare the effects of two oral appliances on upper airway structure.

METHODS

Subjects

Patients with OSA were prospectively recruited from a sleep disorders clinic in a university teaching hospital for treatment with a customized MAS. The study was approved by the institutional ethics committee, and written informed consent was obtained from all patients. Inclusion criteria required a minimum of 2 OSA symptoms (snoring, witnessed apneas, fragmented sleep, and daytime sleepiness) plus confirmation of OSA by polysomnography (apnea-hypopnea index [AHI] ≥ 10 events/h). Patients were excluded if they had periodontal disease, insufficient number of teeth, or an exaggerated gag reflex (contraindications to MAS use).

Oral Appliances

The MAS provided to patients was a custom-made 2-piece appliance (SomnoDent MAS; SomnoMed Ltd, Crows Nest, Australia) with previously published design features and efficacy.[16-21] To enable wear during MRI, the standard adjustable screw mechanism of this appliance was replaced with a modifiable acrylic coupling mechanism.[15] The TSD was a preformed silicon appliance (Aveo-TSD, Innovative Health Technologies, New Zealand).[6] The flanges of the TSD

are placed outside the lips while the tongue is inserted into the bulb. The bulb is squeezed and released to generate suction until the tongue is retained without excessive discomfort. There was no method to standardize the suction pressure of the TSD; however, each patient adjusted the appliance to their own comfort level.

Magnetic Resonance Imaging of the Upper Airway

Magnetic resonance imaging was performed with a Philips INTERA 1.5T MRI scanner (Philips Electronics, Netherlands) while patients were awake, supine, and positioned with the Frankfort plane perpendicular to horizontal as previously described.[15] Scans of each patient were acquired without and with each of the appliances in a randomized order. Contiguous T1-weighted spin-echo images were acquired through the mid-sagittal plane (1.25 mm thickness, 50 slices, 272 × 512 matrix) and axial plane (3 mm thickness, 50 slices, 224 × 12 matrix).

Anatomic Definitions, Measurements and Analysis

MRI data were assessed by the segmentation of upper airway lumen and soft tissue structures and identification of cephalometric landmarks. MR images were processed with image analysis software (Amira 4.1; Visage Imaging Inc., Carlsbad, CA) using previously described and validated techniques.[15,22-24] Upper airway regions were defined as follows: velopharynx (hard palate to tip of uvula), oropharynx (tip of uvula to tip of epiglottis), and hypopharynx (tip of epiglottis to vocal cords) (Figure 1A). The airway lumen was segmented on axial image slices using a region-growing tool of the software, which marks a boundary around a seed point encapsulating pixels below a patient-specific threshold intensity for air (black).[25] Airway volumetric information, as well as cross-sectional area (CSA) and anteroposterior (A-P) and lateral (L) diameters were obtained. Airway shape was calculated by the A-P:L ratio where a ratio of 1.0 represents a circle, while values < or > 1.0 indicate an elliptical shape oriented with the long axis in the coronal or sagittal plane, respectively.[26]

Parapharyngeal fat pads, soft palate, tongue (genioglossus and base of tongue muscles) and lateral pharyngeal wall (retropalatal and retroglossal) were segmented on axial slices (Figure 1B), and reconstructions were used to obtain volumes and assess tissue movements. To assess movement *x*, *y*, z coordinates of the centroid (a point analogous to the centre of mass of an object) of each tissue structure were obtained, and the magnitude and direction of centroid movement with mandibular and tongue advancement determined (Figure 1C).

Cephalometric landmarks were identified on mid-sagittal images. Sella-nasion-A (SNA) angle, sella-nasion-B (SNB) angle, A-nasion-B (ANB) angle, basion-sella-nasion (BaSN) angle, and anterior nasal spine to gnathion distance (ANS-Gn, to measure lower anterior facial height) were obtained. Hyoid to C3 vertebra (H-C3), hyoid to posterior nasal spine (H-PNS), and hyoid to gnathion (H-Gn) distances were used to evaluate hyoid position (Figure 1D).

Polysomnography

All patients underwent polysomnography to determine treatment outcome with MAS. A subset of 18 patients additionally underwent polysomnography with TSD as part of a randomized controlled trial comparing the efficacy of the 2 oral appliances.[6] Findings pertaining to TSD and MAS treatment response are described in this 18-patient subgroup. Polysomnography was scored in accordance with standard criteria.[15,27-29]

Treatment Outcome

Treatment outcome was based on definitions previously described.[16,18,20] In keeping with our previous imaging study,[15] "responders" were defined by ≥ 50% AHI reduction and "non-responders" by < 50% AHI reduction.

Statistical Analysis

Statistical analyses were performed using statistical software package SPSS (version 16.0 for Windows; SPSS, Inc., Chicago, IL). Descriptive statistics for patient clinical characteristics and MRI parameters are presented as mean ± standard deviation (SD) and means ± standard error of the mean (SEM), respectively. Continuous variables between conditions (baseline, MAS, TSD) were compared using repeated-measures ANOVA. If the *F*-statistic indicated a significant difference, paired *t*-tests comparing the 3 conditions were performed with a Bonferroni adjusted α level of 0.05/3 (0.017) (Holm procedure) for each comparison. In cases of non-normally distributed data, a non-parametric test was used (Wilcoxon rank-sum). Differences between treatment responders and non-responders were assessed by Student's *t*-test. Relationships between anthropometric, polysomnographic and airway measurements were assessed with Pearson correlation coefficient, or Spearman correlation coefficient if data were not normally distributed. Statistical significance was accepted at $P < 0.05$.

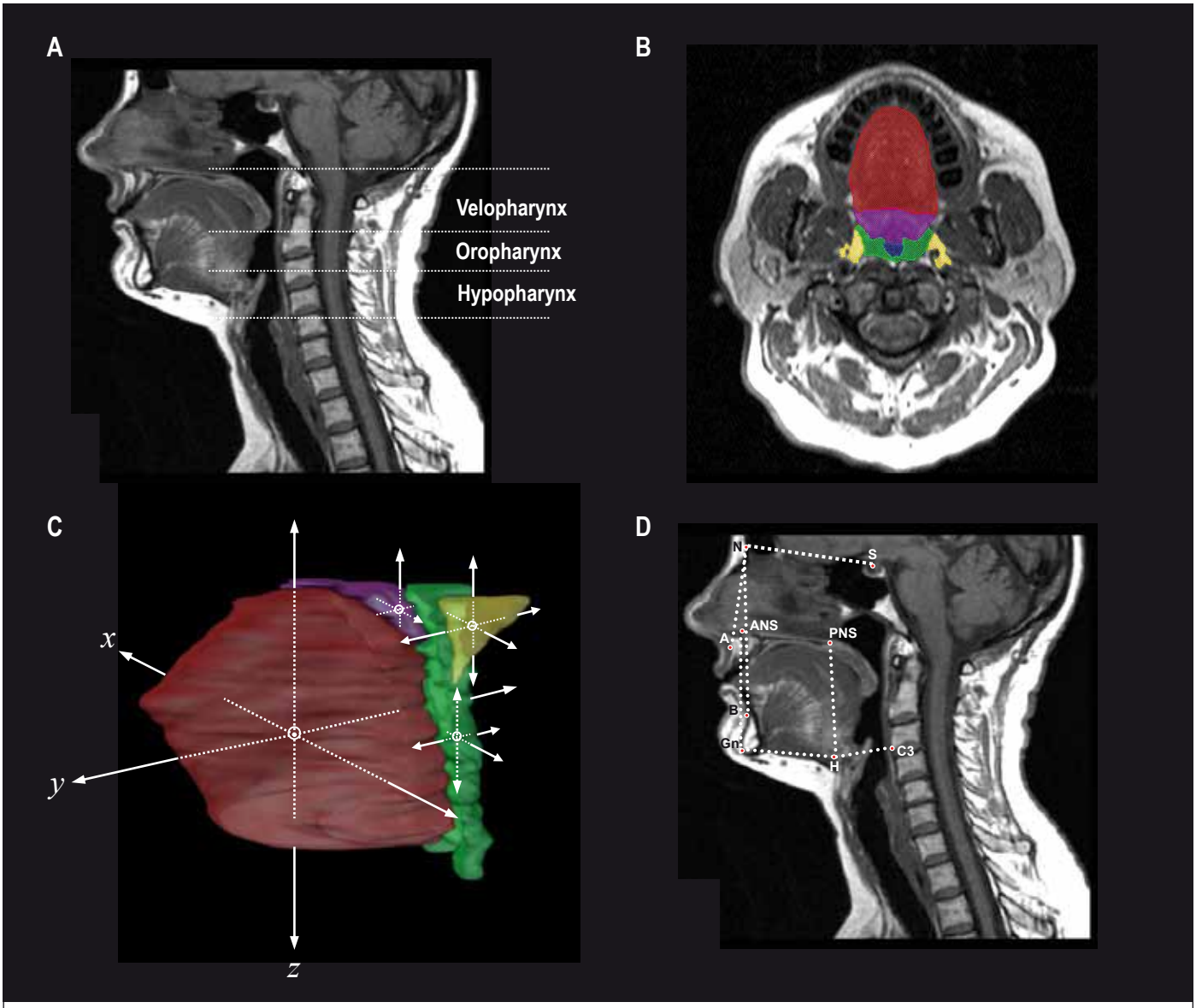

Figure 1—Image analysis. **(A)** Mid-sagittal MRI demonstrating upper airway regions. **(B)** Representative axial MRI illustrating segmentation of upper airway structures; airway lumen (blue), soft palate (purple), tongue (red), parapharyngeal fat pads (yellow), and lateral pharyngeal walls (green). **(C)** Volumetric reconstructions of upper airway soft tissues showing the principle of calculation of magnitude and direction (*x*, *y*, *z*) of centroid movement. **(D)** Cephalometric linear and angular measurements of maxilla, mandible and hyoid position and anterior facial height. S, sella; N, nasion; ANS, anterior nasal spine; PNS, posterior nasal spine; A, A point; B, B point; Gn, gnathion; H, hyoid; C3, C3 vertebra.

RESULTS

Clinical Characteristics

Thirty-nine OSA patients underwent upper airway imaging with both the MAS and TSD. The clinical characteristics of these patients are shown in Table 1. Characteristics of the subgroup of 18 patients who completed overnight polysomnography with TSD did not significantly differ from those who did not.

Comparison of Effects of MAS and TSD on Upper Airway Structure

Airway variables

Airway volume changes with MAS and TSD are shown in Table 2. Volumetric reconstructions of the upper airway from a single patient are shown in Figure 2. There was a small but significant decrease in upper airway length from baseline (8.9 ± 0.2 cm) with both MAS (8.6 ± 0.2 cm; $P < 0.001$) and TSD (8.7 ± 0.2 cm; $P < 0.02$). The effects of MAS and TSD on airway CSA are shown in Figure 3. Both oral appliances increased mean CSA of the total upper airway, but TSD did so to a significantly greater extent. There were regional differences in the effects of both appliances (Figure 3). Lateral and A-P dimensions as well as A-P:L ratio are shown in Figure 4. Both appliances had the greatest effect on velopharyngeal lateral diameter. However, TSD had a larger effect on lateral diameter and additionally increased A-P diameter. Despite this TSD and MAS similarly influenced velopharyngeal shape to be more elliptical with a lateral long axis. This is represented schematically in Figure 4B.

TSD changes in oropharyngeal A-P diameter ($r = -0.32$, $P < 0.05$), oropharyngeal minimum CSA ($r = -0.36$, $P < 0.05$), and hypopharyngeal volume ($r = -0.33$, $P < 0.05$) were inversely

Table 1—Patient characteristics

	n = 39	n = 18
Gender (% male)	64	70
Age (years)	50 ± 10.7	47.7 ± 11.3
BMI (kg/m^2)	29.2 ± 5.5	27.7 ± 5.1
Neck circumference (cm)	39.3 ± 4.2	39.3 ± 4.2
Baseline AHI (events/h)	26.9 ± 17.1	26.8 ± 18.1
Baseline AHI range (events/h)	10.3 – 75.7	10.3 – 75.7
AHI with MAS (events/h)	12.0 ± 12.6	12.0 ± 9.6
AHI with TSD (events/h)	N/A	11.0 ± 9.1
Mandibular advancement (% of maximum)	75.4 ± 14.1	75.6 ± 12.6

Characteristics are shown for the patient sample as a whole (n = 39) and for the subset of these patients who had efficacy data for both oral appliances (n = 18). Mean values ± standard deviation. TSD, tongue stabilizing device; BMI, body mass index; AHI, apnea hypopnea index.

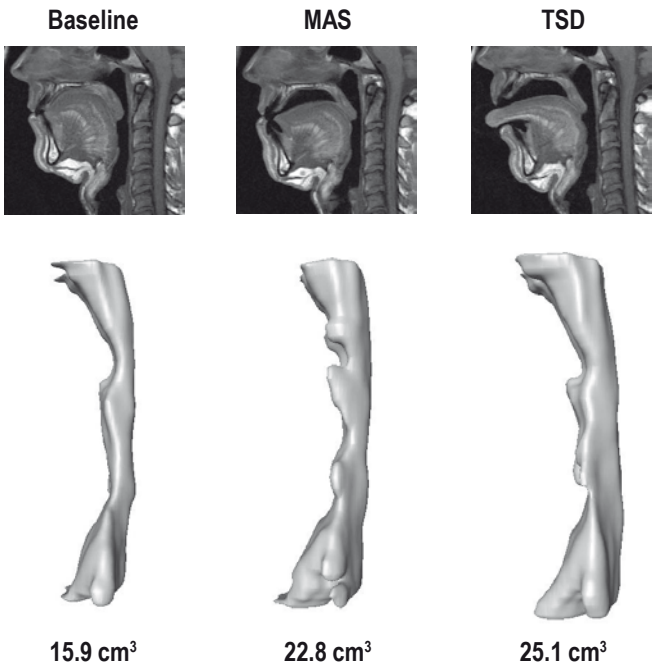

Figure 2—Volumetric reconstructions of the upper airway at baseline and with MAS and TSD in a single OSA patient. Corresponding mid-sagittal magnetic resonance images are shown.

related to BMI. Similarly, changes in A-P diameter (r = −0.455, P < 0.01), lateral diameter (r = −0.331, P < 0.05), and minimum CSA (r = −0.468, P < 0.01) showed inverse relationships with neck circumference. There were no relationships between MAS airway changes and BMI or neck circumference.

Soft tissue centroid movements

Overall centroid movements were relatively small; however, different patterns were observed. Both appliances resulted in lateral movement of the parapharyngeal fat pads away from the airway (MAS 0.28 ± 0.03 cm, TSD 0.23 ± 0.03 cm). Superior displacement of the fat pads was significantly greater with TSD than MAS (0.44 ± 0.05 *vs.* 0.12 ± 0.03 cm; P < 0.001). MAS resulted in slight posterior displacement of the soft palate (0.06 ± 0.03 cm), but TSD produced anterior (0.12 ± 0.03 cm) and superior (0.19 ± 0.04) movement.

TSD moved the tongue further forward than MAS (0.68 ± 0.04 *vs*. 0.06 ± 0.04 cm; P < 0.001). The tongue also moved superiorly with TSD (0.11 ± 0.05 cm) but inferiorly with MAS (0.11 ± 0.06 cm; P < 0.01). Muscles at the base of the tongue shifted forward with MAS (0.35 ± 0.04 cm; P < 0.001).

Velopharyngeal lateral pharyngeal walls moved laterally with MAS (0.14 ± 0.02 cm) and TSD (0.17 ± 0.02 cm). Anterior (0.14 ± 0.02 cm; P < 0.001) and superior (0.2 ± 0.05 cm; P < 0.001) movement also occurred with TSD. The oropharyngeal pharyngeal walls moved more superiorly with TSD (0.32 ± 0.05 *vs.* 0.11 ± 0.05 cm; P < 0.001). The relative movements of upper airway soft tissue centroids are illustrated in Figure 5.

Table 2—Upper airway volume at baseline and with MAS and TSD (n = 39)

	Baseline	MAS	TSD
Total airway (cm^3)	13.8 ± 1.0	14.3 ± 1.1	17.14 ± 1.6*#
Velopharynx (cm^3)	5.1 ± 0.4	5.4 ± 0.5	6.4 ± 0.7*#
Oropharynx (cm^3)	2.9 ± 0.3	3.1 ± 0.3	3.3 ± 0.3
Hypopharynx (cm^3)	5.7 ± 0.5	5.8 ± 0.5	6.4 ± 0.6

Mean values ± standard error of mean. *P < 0.05 *vs.* baseline; #P < 0.05 MAS *vs.* TSD. MAS, mandibular advancement splint; TSD, tongue stabilizing device.

Cephalometric analyses

Cephalometric measurements are shown in Table 3. SNB angle showed an increase with MAS and decrease with TSD. TSD increased lower face height (ANS-Gn) to a greater extent than MAS. Both appliances decreased H-PNS distance, but TSD additionally decreased H-C3 and H-Gn distances.

Upper Airway Structure and Treatment Outcome

In the subset of 18 patients with treatment outcome data, 10 patients were TSD responders and 8 non-responders. Responders and non-responders did not differ in terms of age (46.2 ± 11.7 *vs.* 49.5 ± 11.3 years), BMI (26.3 ± 4.8 *vs.* 30.5 ± 5.4 kg/m^2), or neck circumference (38.7 ± 4.8 *vs.* 41.9 ± 4.1 cm), but baseline AHI did differ (34.8 ± 21.1 *vs.* 16.9 ± 4.5 events/h; P < 0.05). There were no differences between responders and non-responders in baseline upper airway structure (data not shown). However differences were observed in changes in velopharyngeal measurements. Responders showed a greater increase in A-P diameter (+0.2 ± 0.08 vs. –0.08 ± 0.06 cm; P < 0.02), minimum CSA (+0.44 ± 0.2 vs. –0.12 ± 0.1 cm^2; P < 0.05), mean CSA (+0.75 ± 0.2 vs. +0.02 ± 0.2 cm^2; P < 0.01), and volume (+2.65 ± 0.9 vs. –0.44 ± 0.8 cm^3; P < 0.05).

Of these 18 patients, 12 were MAS responders and 6 non-responders. There were no differences in age (47.5 ± 11.8 *vs.* 48.1 ± 11.5 years), BMI (27.0 ± 4.4 *vs.* 30.5 ± 6.7 kg/m^2), neck circumference (40.0 ± 3.9 *vs.* 41.3 ± 5.5 cm), or baseline AHI (30.6 ± 20.7 *vs.* 19.2 ± 8.2 events/h) between MAS response

groups. Baseline or changes in upper airway structure did not differ between MAS responders and non-responders. There was no linear relationship between changes in AHI and airway volume with either appliance (Figure 6). Cephalometric measurements or changes and soft tissue centroid movements did not differ between treatment responders and non-responders for either appliance. In particular, it did not appear that differences in the degree of mouth opening, as assessed by the cephalometric measure ANS-Gn, induced by the 2 appliances had an impact on treatment outcome.

A cross-tabulation of these 18 patients by MAS and TSD response are shown in Table 4. Of these patients, 77.7% had the same category of response (responder or non-responder) with either appliance. There was no correlation between total airway or velopharyngeal volume changes between the two appliances ($r = 0.01$, $P = 0.96$). However, changes in oropharyngeal volume appear to show some consistency between the two appliances ($r = 0.71$, $P = 0.001$).

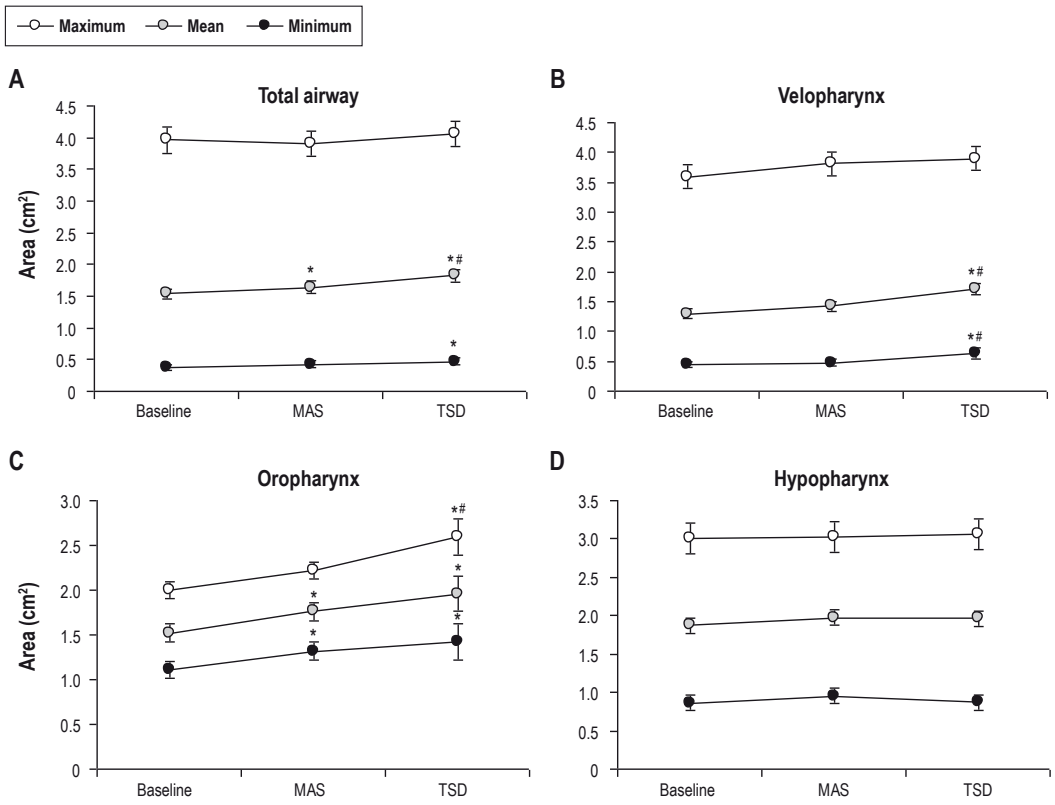

Figure 3—Upper airway cross-sectional area at baseline and with MAS and TSD. **(A)** Total upper airway. **(B)** Velopharynx. **(C)** Oropharynx. **(D)** Hypopharynx. *P < 0.05 *vs.* baseline, #P < 0.05 MAS *vs.* TSD.

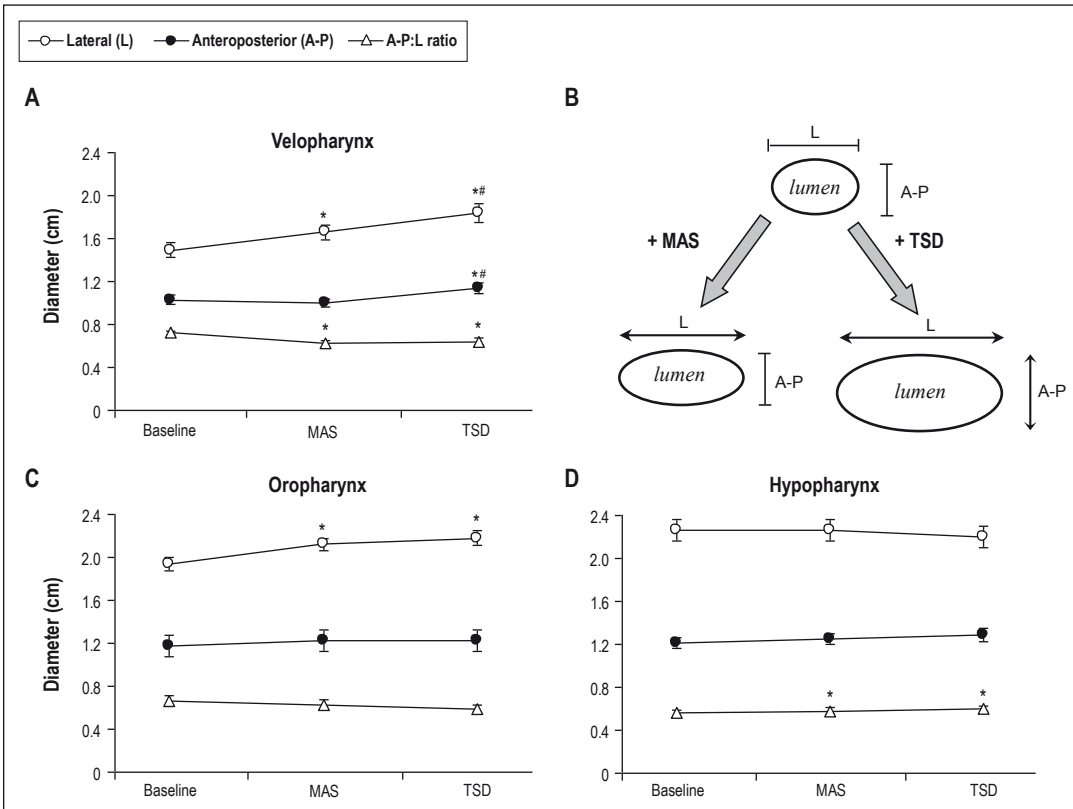

Figure 4—Upper airway lateral (L) and antero-posterior (AP) diameters at baseline and with MAS and TSD. The A-P:L ratio measure of shape is also shown. **(A)** Velopharynx. **(B)** Schematic representation of L and A-P diameter and shape changes in the velopharynx with MAS and TSD. **(C)** Oropharynx. **(D)** Hypopharynx. *P < 0.05 *vs.* baseline, #P < 0.05 MAS *vs.* TSD.

DISCUSSION

This is the first study to compare the effects of two oral appliances, MAS and TSD, on upper airway structure using MRI. Clinically MAS are more widely used and investigated, while TSD have received less attention, and their role in OSA treatment remains uncertain. Our results indicate that both MAS and TSD increase upper

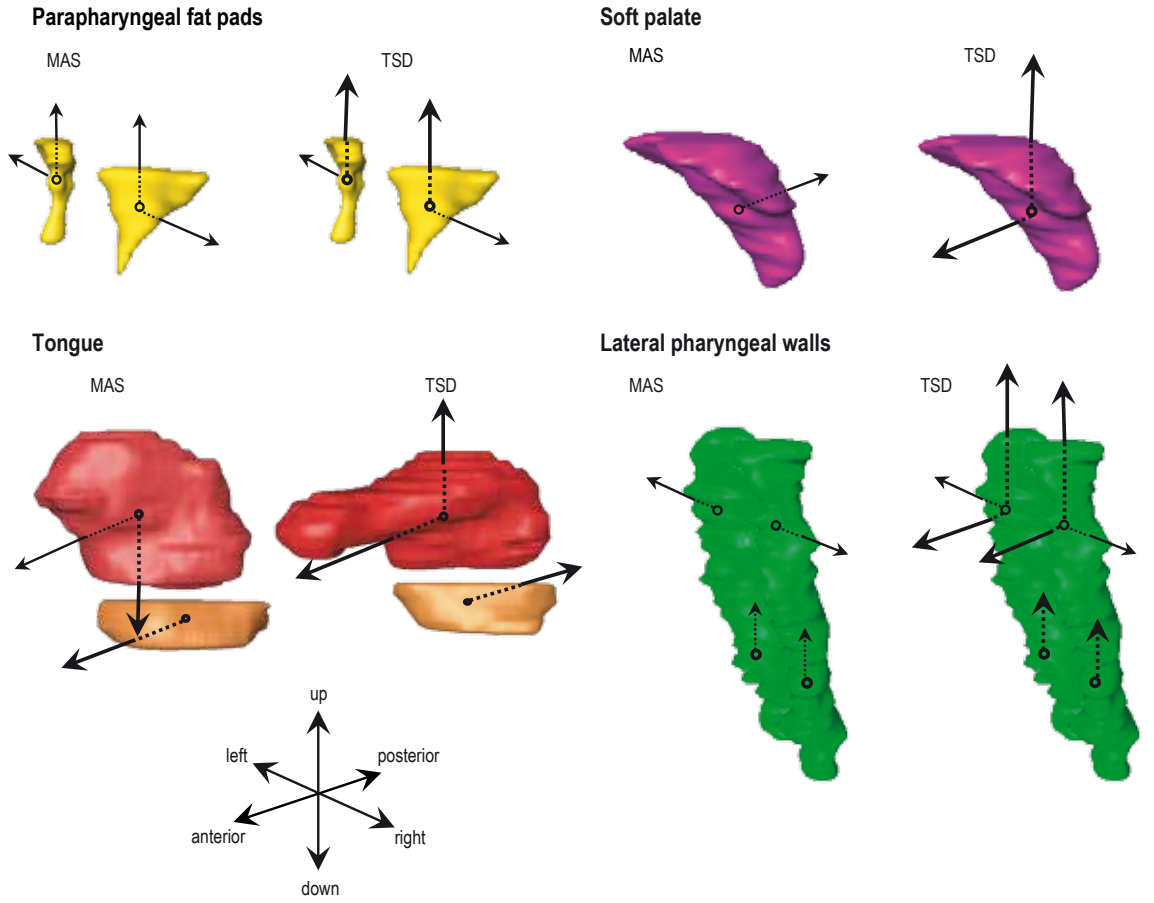

Figure 5—Schematic representation of soft tissue centroid movements with MAS and TSD. Larger and bolder arrows represent significantly greater centroid movements with each appliance.

Table 3—Cephalometric measurements at baseline and with MAS and TSD (n = 39)

	Baseline	MAS	TSD
SNA (°)	82.9 ± 0.8	83.4 ± 0.7	83.3 ± 0.8
SNB (°)	79.8 ± 0.8	82.0 ± 0.8*	76.2 ± 0.8*#
ANB (°)	3.0 ± 0.8	1.4 ± 0.7*	7.1 ± 0.7*#
ANS-Gn (cm)	6.9 ± 0.1	7.6 ± 0.1*	8.7 ± 0.1*#
H-C3 (cm)	3.8 ± 0.1	3.8 ± 0.1	3.7 ± 0.1*#
H-PNS (cm)	7.4 ± 0.1	7.1 ± 0.1*	7.2 ± 0.1*
H-Gn (cm)	4.6 ± 0.1	4.7 ± 0.1	4.2 ± 0.1*#

Mean values ± standard error of mean. *P < 0.01 *vs.* baseline; #P < 0.01 MAS *vs.* TSD. SNA, sella-nasion-A point; SNB, sella-nasion-B point; ANB, A point-nasion-B point; ANS-Gn, anterior nasal spine to gnathion distance; H-C3, hyoid to C3 vertebra distance; H-PNS, hyoid to posterior nasal spine distance; H-Gn, hyoid to gnathion distance.

Table 4—Cross-tabulation showing treatment response with MAS and TSD (n = 18)

	MAS outcome		TSD Total
TSD outcome	Responder	Non-responder	
Responder	9	1	10
Non-responder	3	5	8
MAS Total	12	6	18

airway dimensions but that there are differences in their effects on upper airway structure. Overall TSD have a greater effect on upper airway size than MAS.

Previous imaging studies of tongue protrusion are limited. A nasopharyngoscopic investigation of voluntary tongue and mandible protrusion[30] reported a greater increase in velopharyngeal and oropharyngeal CSA with tongue compared to mandible protrusion, which is in accordance with the findings of the current study using oral appliances. The greater effects of TSD on upper airway structure may be a result of this appliance mechanically producing more anterior movement of the tongue. This action of protruding the tongue outside the oral cavity may cause greater displacement of other tissues. The level of mandibular advancement achieved with MAS averaged 6 millimeters, and therefore effects on upper airway structures may be more subtle.

This comparative imaging study suggests both appliances primarily improve upper airway caliber in the velopharynx. The velopharynx is the most common site of primary pharyngeal collapse in OSA.[31,32] Increased velopharyngeal lateral diameter appears to be the main effect of MAS on the upper airway.[12,15] This is likely a consequence of stretching soft tissue connections between the tongue, soft palate, and lateral pharyngeal walls

through the palatopharyngeal and palatoglossal arches.[10,33] Although TSD increases airway A-P diameter via forward displacement of the tongue, traction on these intra-pharyngeal connections via the tongue base may additionally increase the lateral dimension. The primarily lateral airway increase with both appliances and subsequent shape change to an ellipse in this orientation may favor reduced collapsibility. These data are consistent with respiratory-related changes in the airway that occur primarily in the lateral rather than A-P direction, suggesting more compliant lateral walls.[25,34]

A significant reduction in upper airway length was noted with both appliances. However, as mean length change was less than image slice thickness, this airway length change requires further investigation. Nonetheless, pharyngeal length has been shown to increase in OSA patients when supine,[35] and reduction in pharyngeal length with oral appliances may represent a potential mechanism of action. Superior movement of the hyoid bone towards the posterior nasal spine was also associated with both appliances. An inferiorly positioned hyoid bone is a cephalometric variable commonly associated with OSA.[36,37] It is unclear whether the inferiorly positioned hyoid is a cause or result of OSA; however, it appears that oral appliances have a corrective effect on hyoid position.

We have previously shown differences in the effects of MAS related to treatment outcome with improved airway caliber only evident in responders (although in the patient subset analyzed in this study these differences were not significant).[15,29] In this study we were able to demonstrate significant increases in velopharyngeal airway dimensions with TSD in treatment responders only, suggesting efficacy is related to improved airway caliber. However, there is no direct linear relationship between changes in airway structure and improvement in total AHI with either appliance. This is not completely surprising and may relate to issues with night-to-night variability in AHI and sleep positions, and the relationship between upper airway size and OSA severity itself is unlikely to be linear.

In this sample, ~77% of patients showed an equivalent treatment response with both appliances suggesting that some patients may characteristically respond to either form of oral appliance. We did identify a moderate correlation between the changes in oropharyngeal volume produced with both appliances. Previous studies have found that site of pharyngeal collapse is a significant determinant of treatment outcome, with patients who have primary oropharyngeal collapse more likely to respond to treatment.[38,39] In the current study, oropharyngeal improvements were similar with both appliances and may explain why TSD (which improved velopharyngeal dimensions significantly more than MAS) was not more efficacious. Nevertheless, although structural characteristics are likely to be relevant, neuromuscular factors may additionally be important. Indeed a normalizing effect of TSD on the time lag between peak inspiratory genioglossus muscle activity and maximum inspiratory effort during apneic events has been demonstrated[40] and is dependent on active retention of the tongue in the bulb.

The "holy grail" in terms of oral appliance treatment is the ability to predict which patients will respond to treatment. In our previous MRI study with MAS there were no baseline upper airway structures that allowed discrimination between responders and non-responders. Similarly, this study revealed no baseline characteristics related to TSD treatment response. However, there appears to be some relationship between BMI and neck circumference and the effect of TSD on upper airway size, with smaller body measures indicative of a greater improvement in measures of airway caliber. Larger body measures may be indicative of excess soft tissue surrounding the upper airway, which cannot be easily displaced to effectively increase upper airway size with TSD.

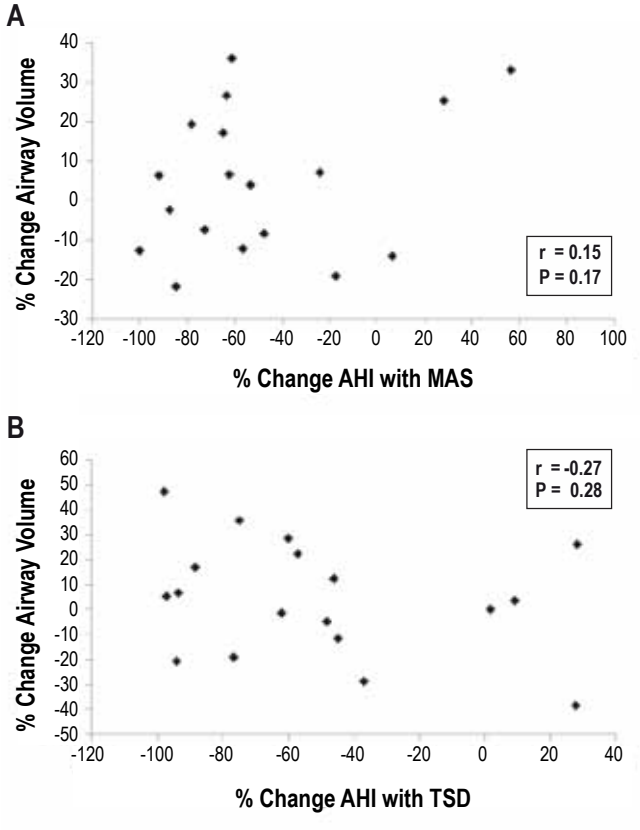

Figure 6—Changes in total airway volume and AHI with oral appliance treatment. **(A)** MAS. **(B)** TSD. There was no significant relationship between airway size and treatment efficacy with either appliance. N = 18.

We have previously demonstrated that MAS and TSD similarly improve AHI.[6] However MAS is effective in a greater proportion of patients and is additionally associated with greater symptomatic improvement, compliance, and patient preference. This may relate to issues with wearing the TSD, such as discomfort and involuntary removal during sleep, which result in reduced usage time. Therefore although TSD appears to have more favorable effects on upper airway caliber than MAS, practical issues may circumvent these positive effects. However, for patients who are able to tolerate TSD or are not suitable for MAS treatment, this study demonstrates highly favorable effects of this device on upper airway structure. Although TSD are not commonly used in clinical practice, a role for this type of appliance has previously been proposed for patients in whom MAS is contraindicated, such as those with insufficient teeth to retain the appliance or those with periodontal disease. Patients in this study had to be suitable candidates for MAS therapy, and therefore all patients had enough teeth to use MAS. How airway structural changes and efficacy with TSD are affected by issues such as edentulism would need to be addressed by future studies.

There are some limitations to this study. The MAS used was modified by removing the screw mechanism in order to permit imaging, and this appears to have resulted in lesser degrees of mandibular advancement than reported in our earlier efficacy studies.[16,17,19] Hence this may have attenuated the airway changes observed with MAS in the current study. Image acquisition with MRI occurs over many minutes, and therefore the data represent averages across respiratory cycles. Imaging was performed during wakefulness, and the effects of MAS and TSD on upper airway structure may not be identical during sleep. However, imaging during sleep is technically challenging, and valuable insights can be gained using awake imaging as a surrogate.[23] TSD application was not standardized; therefore, degree of tongue protrusion may not have been consistent between the sleep study and image acquisition. However, this only affects results related to treatment outcome. Moreover, the use of TSD in this manner reflects the intended use by the manufacturer as the appliance is commercially available. Relating our supine imaging findings to treatment outcome based on total AHI may not be completely applicable. Airway shape, in both OSA patients and healthy controls, changes from an ellipse while supine to more circular in the lateral recumbent position.[41] What effect posture has on airway dimensions with oral appliances has not been investigated. It is possible that effects on airway dimensions and efficacy may differ with body position; however, both appliances reduce supine and non-supine AHI.[6] Although we employed a novel method to examine soft tissue movements by measuring displacement of the structure's centroid, this is likely to be an oversimplification, which neglects morphological changes that require more complex analysis methods. Nonetheless this method was able to detect differences in soft tissue movements between MAS and TSD, giving insight into the differential structural effects of these oral appliances.

In conclusion both MAS and TSD increase upper airway dimensions and move surrounding soft tissues; however, the magnitude and pattern of changes differ between appliances. Further research evaluating whether these changes or the site of change within the airway can be used to predict treatment outcome is warranted.

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DISCLOSURE STATEMENT

The oral appliances used in this study were provided at no cost by SomnoMed Ltd. Australia (mandibular advancement splints) and Innovative Health Technologies Ltd., New Zealand (tongue stabilizing devices). These companies had no other role in the study. Dr. Cistulli contributed to the development of the mandibular advancement splint used in this study. He has consulted for and has been on the advisory board of SomnoMed. He is a consultant for ExploraMed and has financial interest in the company. His department has received research support from ResMed and SomnoMed. He is a board member of the ResMed Foundation, a nonprofit, charitable organization. Dr. Schwab has participated in speaking engagements for Nuvigil. The other authors have indicated no financial conflicts of interest.

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Comparison of Mandibular Advancement Splint and Tongue Stabilizing Device in Obstructive Sleep Apnea: A Randomized Controlled Trial

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Study Objectives: To compare the efficacy of a mandibular advancement splint (MAS) and a novel tongue stabilizing device (TSD) in the treatment of obstructive sleep apnea (OSA).

Design: A randomized crossover design was used.

Patients: Twenty-seven patients (20 male, 7 female), recruited from a tertiary hospital sleep clinic.

Measurements and Results: The apnea-hypopnea index (AHI) was reduced with MAS (11.68 ± 8.94, P = 0.000) and TSD (13.15 ± 10.77, P = 0.002) compared with baseline (26.96 ± 17.17). The arousal index decreased for MAS (21.09 ± 9.27, P = 0.004) and TSD (21.9 ± 10.56, P = 0.001) compared with baseline (33.23 ± 16.41). Sixty-eight percent of patients achieved a complete or partial response with MAS, compared with 45% with TSD. The Epworth Sleepiness Scale (ESS) score was decreased with MAS (P = <0.001) and TSD (P = 0.002). Subjective improvements in snoring and quality of sleep were reported, with a better response for MAS than TSD. Compliance was poorer for TSD, and the side effect profiles of the 2 modalities were different. All patients were satisfied with MAS compared to TSD, and 91% of patients preferred the MAS.

Conclusion: Objective testing showed the MAS and TSD had similar efficacy in terms of AHI reduction. Patients reported improvements with both devices; however, better compliance and a clear preference for MAS was apparent when both devices were offered. Longer term studies are needed to clarify the role of TSD.

Keywords: mandibular advancement splint, tongue stabilizing device, obstructive sleep apnea

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OBSTRUCTIVE SLEEP APNEA (OSA) IS A COMPLEX MULTIFACTORIAL CONDITION PRODUCED BY A COMBINATION OF ANATOMIC AND PHYSIOLOGICAL FACTORS.[1] It is characterized by repetitive complete or partial closure of the upper airway during sleep resulting in sleep fragmentation and oxygen desaturation.[2,3] Numerous risk factors including male gender and obesity,[4] ethnicity,[5] and craniofacial structure[6] have been identified as increasing susceptibility to this disease. OSA has a significant associated morbidity and mortality and has been linked to cardiovascular[7,8] and cerebrovascular disease,[9,10] excessive daytime sleepiness,[11] and increased risk for motor vehicle accidents.[12-14] The prevalence of OSA varies depending on diagnostic criteria and population studied, and has been reported as affecting 4% of men and 2% of women in the middle-aged workforce.[15] It was also found that among adults aged 30-69 years, 17% of adults had mild or worse sleep disordered breathing (AHI ≥ 5), and 5.7% of adults had moderate or worse sleep disordered breathing.[16] As such, OSA is recognized as a significant public health issue.

While the gold standard of care combines conservative modalities such as weight loss and nasal continuous positive airway pressure (CPAP),[17] interest in oral devices has been increasing possibly because of compliance difficulties with CPAP. Mandibular advancement splints (MAS) are the most common type of oral device; they protrude the mandible during sleep, thereby having a favorable impact on upper airway structure and function. Several designs have been extensively investigated and shown to be efficacious in a substantial number of patients, particularly those with mild to moderate OSA.[18-21] The American Academy of Sleep Medicine practice parameters recommend the use of MAS as an alternative to CPAP for patients who prefer oral appliances or refuse or are unable to tolerate CPAP, particularly in mild to moderate OSA.[22] A tongue stabilizing device (TSD) is a preformed appliance and uses suction to protrude the tongue and improve upper airway structure and function. The earlier designs were similar to a mouthguard, covering the upper and lower teeth to assist retention, with a flexible bulb into which the tongue was protruded.[23] The current design has no dental coverage, reduced bulk, and has the bulb being retained in place only by suction. There are currently only limited data on the efficacy of the current device, which is commercially available.[24] As they are not reliant on the teeth for retention, TSD have been proposed as an option for patients with a reduced number or absence of teeth (hypodontia, edentulism), or compromised dental health (periodontal disease). The aim of this study was to compare the efficacy of these 2 types of oral devices in typical OSA patients.

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METHODS

Subjects

Twenty-seven patients were recruited from a sleep clinic in a university teaching hospital. The study was approved by the

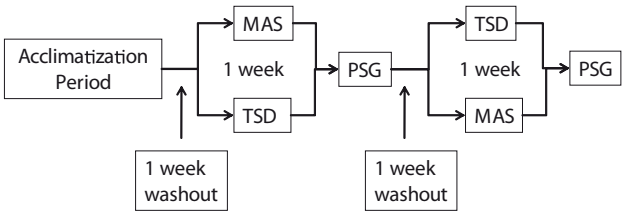

Figure 1—Schematic diagram summarizing the study design. PSG = polysomnography.

institutional ethics committee, and all patients were provided with written informed consent. Inclusion criteria were age > 20 years, ≥ 2 symptoms of OSA (snoring, fragmented sleep, witnessed apneas, daytime sleepiness) and evidence of OSA on polysomnography with an apnea hypopnea index (AHI) > 10 per hour. Exclusion criteria were regular use of sedative medications, previous failure of an oral appliance for treatment of OSA, exaggerated gag reflex, edentulous patients, and < 10 teeth per jaw or evidence of periodontal disease.

Experimental Design

A randomized crossover design was used (Figure 1). The patients had an 8-week acclimatization period (4 weeks with each device), during which they were provided with the devices in random order and asked to complete questionnaires. Patients subsequently underwent 1-week intervention with each treatment in random order. One-week washout periods were applied prior to and between the treatment phases. Overnight polysomnography was performed with the designated device at the end of each 1-week treatment phase as per previous studies.[18,19]

Two types of oral appliances were provided to the subjects. The MAS was a custom-made 2-piece device (Somnomed Ltd, Australia) with vertical extensions on the lower component and ramps on the upper component which induced a forward mandibular posture as previously described (Figure 2).[18,20] For the current study, a non-titratable version of the device was used by not incorporating the usual adjustable screw mechanism. This was to permit patient participation in a separate magnetic resonance imaging research study with the device. A protrusive bite was taken with a 4-mm vertical interincisal opening at 75% of the maximal comfortable protrusive range.[18] Patients were instructed on insertion and removal of the MAS and advised to wear it during the sleeping period as much as possible. The tongue stabilizing device used in this trial was a preformed, non-adjustable silicon appliance constructed by injection molding (Aveo-TSD, Innovative Health Technologies, New Zealand) (Figure 3). Patients were instructed to rinse the device with water, place the flanges of the TSD on the outside of the upper and lower lips, insert the tongue into the bulb as far as was comfortable, then squeeze and release the bulb to generate suction. Patients were advised to increase the suction by protruding the tongue further and/or squeezing the bulb more should the device loosen or be insufficiently retentive, or decrease the suction should there be excessive discomfort.

Figure 2—Photograph of upper and lower plates of the mandibular advancement splint.

Treatment Outcome

The primary outcome for treatment efficacy was the apnea-hypopnea index (AHI) derived from standard nocturnal polysomnography (Compumedics Limited, Australia). Also measured were total sleep time, sleep time in REM, sleep time in NREM, arousal index (AI), sleep efficiency, minimum oxygen saturation ($MinSO_2$), longest apnea, longest hypopnea, and mean duration of apneas and hypopneas. Apnea was defined as a cessation of airflow ≥ 10 s with oxygen desaturation > 3% and/or associated with arousal. Hypopnea was defined as a reduction in amplitude of airflow > 50% of the baseline tidal volume for > 10 s with an accompanying oxygen desaturation of ≥ 3% and/or associated arousal. Nasal airflow was measured using nasal prongs attached to a pressure transducer. Studies were scored by an experienced technician who was blinded to the treatment device.

OSA severity was classified according to the baseline AHI. Mild was defined as an AHI 5 to 15/h, moderate as AHI 15-30/h, and severe as AHI > 30/h. Treatment outcome was classified as follows: complete response (CR) was defined as a resolution of symptoms and a reduction in AHI to ≤ 5/h; partial response (PR) as an improvement in symptoms and ≥ 50% reduction in AHI, but where AHI remained > 5/h: and treatment failure (F) was defined as ongoing clinical symptoms and/or reduction in AHI < 50%. Compliance failure was defined as a patient who discontinued treatment.

Secondary outcomes were assessed using a standardized questionnaire used in our previous published studies.[18,19] These included subjective snoring frequency and intensity, quality of sleep, daytime sleepiness,[25] side effects, patient satisfaction, and appliance preference. Each questionnaire was completed by the patient at the end of the acclimatization phase after wearing each device for 1 month. Compliance, assessed by the number of weeks the patient wore the device in the 1 month available to acclimatize to each device, was also investigated.

Statistical Analysis

Data were analyzed using SPSS (Version 14 and 16). The polysomnographic results were subjected to paired Student's t-Tests to demonstrate any difference between MAS and TSD. Cross tabulation and Pearson χ^2 tests (using linear-by-linear P

Figure 3—Photograph of the tongue stabilizing device.

value) compared the percentage of patients within treatment outcome categories by appliance and OSA severity, as only 2 devices were involved. Analysis of variance (ANOVA) was used to test for period and order effects. All descriptive statistics are presented as mean ± standard deviation. The results of the questionnaires were assessed graphically. Due to the large number of tests carried out with unknown dependence, and allowing for multiple tests, we replaced the standard significance level of 0.05 with a P value of < 0.01. A priori power calculation indicated that a sample size of 21 subjects was required to give a 90% power to detect a 50% reduction in AHI (P = 0.05), based on the data from our group's previous study.[18]

RESULTS

Out of 27 patients initially recruited, 22 patients (16 male, 6 female) completed the protocol. Two patients failed to complete the study for medical and work-related reasons, and 3 patients attended the first consultation, then subsequently withdrew for personal and time concerns unrelated to the nature of the devices. The demographics and baseline data for the patients who completed the protocol (16 male, 6 female) are demonstrated in Table 1. Five patients had mild OSA, 11 had moderate OSA, and 6 had severe OSA. As 50% (3) of the female patients and 19% (3) of the male patients were classified as severe OSA, males and females were grouped together for analysis. The mean anteroposterior mandibular advancement with MAS was 77% of maximum protrusion (mean 4 mm, range 2-10 mm). There was no significant difference in body mass index (BMI) between severity groups.

Results of the polysomnography are detailed in Table 2. A decrease in AHI was recorded for 91% of the patients when using MAS and 77% of the patients when using TSD. Analysis of the effect of the appliances on AHI in supine and other body positions during sleep demonstrated that AHI between baseline and TSD, and baseline and MAS were significantly different (P < 0.001 in each case). There was a marginally significant reduction in REM sleep between baseline and TSD (P = 0.056), and between baseline and MAS (P = 0.051), but not between TSD and MAS (P = 0.72). Subgroup analyses comparing males and females demonstrated little difference between MAS and TSD (data not shown). Of note, in 2 patients the TSD was only tolerated for less than 2 hours during the polysomnographic study.

The treatment outcome with MAS demonstrated that 27.3% had a complete response, 40.9% had a partial response, and

Table 1—Patient Characteristics at Baseline

	Mean ± SD	Range
Age (years)	49.4 ± 11.0	24.8-65.3
Body mass index (kg/m^2)	29.3 ± 5.6	20.6-38.3
Baseline AHI (/h)	27.0 ± 17.2	10.3-75.7
Baseline $MinSaO_2$ (%)	84.3 ± 6.5	71-95

AHI = apnea-hypopnea index; $MinSaO_2$ = minimum oxygen saturation.

31.8% failed. With TSD 22.7% had a complete response, 22.7% had a partial response, and 54.5% failed. Linear-by-linear χ^2 tests demonstrated a trend towards a significant difference between TSD and MAS (P = 0.06). When assessing treatment outcome with both appliances compared with the patients OSA severity, no significant difference (exact linear-by-linear) was detected between the mild, moderate and severe OSA groups (MAS, P = 0.71; TSD, P = 0.23). Table 3 compares the number of patients in each category of treatment outcome for MAS and TSD. There were no significant period or order effects. Although the analysis showed that there was significant interpersonal variability, there was not enough difference between the 2 appliances to reach significance.

Snoring frequency improved from 81.8% of patients snoring 5-7 nights per week at baseline to 11.1% with MAS and 13.6% with TSD. MAS eliminated snoring in 40.9% of patients compared with 27.3% for TSD according to patient's perception. With MAS all patients reported improvement in snoring severity, with 27.3% being very much improved and 59.1% being much improved. With TSD, fewer patients indicated a favorable change in snoring severity, with 13.6% being very much improved, 13.6% being much improved, and 22.7% reporting no improvement. As an indicator of daytime sleepiness, the Epworth Sleepiness Scale (ESS) score decreased significantly with MAS (3.50 ± 2.41, P = 0.000) and TSD (5.86 ± 4.63, P = 0.002) compared with baseline (8.55 ± 5.12). Subjective compliance was better for MAS, with regular use (every night of the week for ≥ 6 h per night) reported by 81.8% of patients, compared with 27.3% for TSD (Figure 4). The incidence of patients involuntarily removing MAS during the night was 9% compared with 86.4% with TSD. At the 4-week follow-up appointment, MAS use was reported by 86.4% of the patients after 3 weeks, whereas 63.6% of patients discontinued use of TSD by 3 weeks. Side effects caused by MAS were jaw discomfort (59.1%) and dryness of mouth (50%), compared with TSD, with which excess salivation (86.4%), dryness of mouth (59.1%), and soft tissue irritation (50%) were problematic. All patients were satisfied with MAS, and 90.9% of patients preferred this device. Satisfaction with the TSD was indicated by 59.1% of the patients, with 3 patients being very dissatisfied.

DISCUSSION

Oral appliances are increasingly being used in the management of OSA. The MAS is the more widely investigated oral appliance with an abundance of literature supporting its use in the management of OSA patients, particularly those with mild

Table 2—Comparison of Polysomnographic Variables Between Baseline, MAS, and TSD

Variable	Baseline Mean ± SD	MAS Mean ± SD	P Value	TSD Mean ± SD	P Value
TST, min	400 ±51	347 ± 77	ns	320 ± 97	ns
REM sleep, min	53 ± 22	63 ± 28	ns	53 ± 31	ns
NREM sleep, min	286 ± 41	283 ± 64	ns	269 ± 76	ns
Arousal index/h	33 ± 16	21 ± 9	0.004	21 ± 11	0.001
Sleep efficiency %	80 ± 11	78 ± 17	ns	79 ± 11	ns
AHI/h	27 ± 17	12 ± 9	0.000	13 ± 11	0.002
$MinSaO_2$ %	84 ± 7	87 ± 5	ns	88 ± 6	ns

TST = total sleep time; AHI = apnea hypopnea index; $MinSaO_2$ = minimum oxygen saturation.

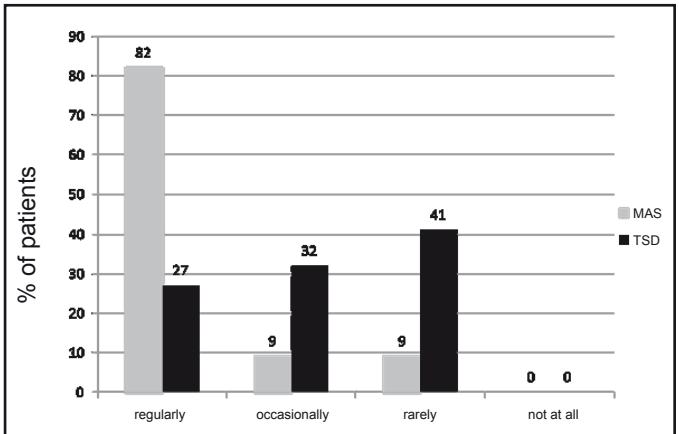

Figure 4—Comparison of compliance frequency reported by patients using MAS and TSD.

Table 3—Cross-Tabulation Showing Treatment Response with MAS and TSD

	MAS Response			Total
	Complete	Partial	Failure	
TSD Response				
Complete	3	1	1	12
Partial	1	4	0	5
Failure	2	4	6	5
Total	6	9	7	22

to moderate OSA.[18-20,26] Across a number of studies, complete and partial response to MAS have been demonstrated in an average of 65% of OSA patients.[27] There is good understanding of the indications for the prescription of MAS and supervising this treatment modality. In contrast, the role of TSD remains uncertain due to a paucity of evidence, with a limited number of studies with small sample sizes and using several appliance designs.[24,28-30] In our short-term randomized controlled study, we demonstrated that MAS and TSD had similar effects on AHI, but that MAS was associated with greater symptomatic improvement, compliance, and patient preference.

The primary outcome in this study was AHI; we found that it decreased in 91% of patients when using MAS and 77% of patients when using TSD.

The present study is the first comparative study for TSD and demonstrates that TSD can yield an improvement in AHI, although in a lesser percentage of patients than MAS. Treatment outcome in this study was based on rigorous definitions, as previously reported by our group, which is a strength of our study. The percentage of patients with complete and partial response for TSD was lower than MAS, although this did not quite reach statistical significance. In addition the arousal index decreased significantly with MAS and TSD which is consistent with previous studies on MAS[18,19,31] and TSD.[24]

The MAS used in this study has been rigorously evaluated in previous studies. In contrast to previous studies of this device, we used a titration strategy aimed at achieving mandibular advancement at approximately 75% of maximal jaw protrusion, rather than the maximal comfortable limit of advancement. This was because the MAS design was modified to remove the titration screws for the purpose of undertaking MRI scans in a separate study. An actual advancement of 77% ± 8% (range 2-10 mm) was achieved in this study. An important limitation of this study was that patients did not have further mandibular advancement as they acclimatized to MAS, which may have limited improvement in OSA in some patients. In support of this possibility is the lower complete response rate than previously reported by studies using this MAS design. Despite this limiting factor, the MAS provided significant clinical benefit.

The TSD appliance was non-adjustable, with the patient controlling the amount of tongue protrusion and suction generated by the device. It was noted that patients protruded the tongue into the appliance by differing amounts and squeezed the bulb with differing force. There was no method to standardize the application of TSD, with each individual having to establish his or her own comfort level. The forward tongue posture and stretching of the related soft tissues (especially the lingual frenum) may have caused discomfort, which in turn may have limited the amount of tongue protrusion and their potential response to TSD. The use of TSD in this manner reflects the real-life use of the device, which is intended by the manufacturer to be available over the counter for use in an unsupervised manner. We believe that clinical supervision is required to ensure patient safety and optimal outcome.

When the sequence of appliance provided first in the acclimatization and trial phases was considered, no significant difference was detected in the treatment outcome, although there was variation between individuals. It was observed that patients who were provided with the TSD as their first device were more willing to persist with the appliance than those who received MAS first, and subsequently appeared less enthusiastic about

TSD. Patients appeared to find the MAS more comfortable and easier to manipulate than the TSD. In addition, 13 of 22 patients achieved the same category of response to treatment with both MAS and TSD. This suggests that some patients may consistently respond to either form of oral appliance. and raises the issue of predictive parameters that could be used to identify such "responders."

Subjective evaluation of snoring frequency and severity showed both MAS and TSD were regarded by the patients (and their partners) as providing an improvement, however TSD was reported to produce less improvement than MAS. O'Sullivan and colleagues[32] found a reduction of 18% in snoring frequency and 15.8% in snoring intensity using MAS. Kingshott and colleagues[24] found the TSD significantly reduced snoring frequency in the 61-70 decibel range, but did not alter snoring in other decibel ranges.

Quality of sleep was improved with oral appliance therapy as has been demonstrated in other studies.[18,27,33] Mehta et al.[18] demonstrated a combined improvement in snoring, sleep quality and daytime sleepiness in 83% of the patients with MAS. In an evidence-based review of 87 articles by Ferguson et al,[27] it was concluded that effects on sleepiness and quality of life were apparent yet improvements in other neuro-cognitive outcomes were less consistent when using oral appliances. In this study all patients reported improvement in quality of sleep with MAS, compared with 45% with TSD.

Objective compliance with oral appliances in the management of OSA is difficult to ascertain. While there has been a report of an objective compliance measuring device, this is not routinely available.[34] Hence we relied on self-report for this study. Compliance, as indicated by the number of nights per week worn (minimum 6 hours per night), was assessed over a 4 week period and divided into 4 groups: regularly (worn every night of the week), occasionally (worn 3-4 nights of the week), rarely (worn 1-2 nights of the week), and not at all (device never worn). Compliance was better for MAS and was comparable to other MAS studies. Mehta and colleagues[18] reported a compliance rate of 87.5% with MAS at one month. There is no literature to assess compliance with TSD but it can be assumed that like MAS, compliance rates are likely to decrease relative to the length of follow-up. To further appreciate the compliance issues patients were asked if they unknowingly removed the appliances during the night. Patients involuntarily removed MAS during the night in 9% of cases compared with 86.4% of cases for TSD, with the device often ending up on the bedside table. This was further evidenced by the fact that 2 patients were only able to tolerate the TSD for less than 2 hours during the efficacy polysomnograph. This appears to be a major limitation of TSD. In addition, MAS use was reported by 86.4% of the patients after 3 weeks, however 63.6% of patients discontinued use of TSD by 3 weeks. Patient satisfaction is likely to be a key influencer of compliance. In our short-term study all patients were satisfied with MAS and 91% of patients preferred this device. Satisfaction with TSD was indicated by only 60% of the patients, with 3 patients being very dissatisfied.

Both MAS and TSD resulted in patients reporting side effects, with each appliance producing a different type and severity of problems. For MAS the main concerns were jaw discomfort (59%) and dryness of mouth (50%). These side effects were largely mild in nature, resolved within about 30 minutes of removing the device, did not persist beyond 1 to 2 weeks and did not prevent the patients from using the MAS. The main side effects caused by TSD were reported as excess salivation (86.4%), dryness of mouth (59.1%), and soft tissue irritation (50%). The problems generated with TSD varied from mild to severe in nature, and appeared to persist for up to or longer than 3 weeks. Several patients described a temporary tingling sensation to the tongue lasting approximately 30 minutes to 1 hour. Minor ulceration of the lingual frenum also occurred, and was addressed by enlargement of the "notch" to accommodate the frenum. If the patient's lingual frenum inhibited their ability to protrude their tongue into the TSD, their response may have been suboptimal and in turn affected compliance. Patients also indicated swallowing was more difficult with TSD due to the vertical mouth opening. The reduction of AHI in supine sleep and slight reduction in REM sleep may have been influenced by the side effects, in particular excess salivation, however there was no statistically significant difference between MAS and TSD. The side effects were severe enough to prevent nearly half of the sample continuing with the TSD, compared with MAS where the side effects did not prevent any of the subjects from using the device.

Our study had a number of potential limitations. The sample population was recruited from a sleep disorders clinic known for its research interest in dental treatments for OSA, and this could have resulted in a referral bias. As the characteristics of the sample population were consistent with other sleep apnea populations reported in the literature, it would appear that bias was minimal. Our sample size was small, raising the possibility of a type 2 error, although our priori sample size calculation suggested the sample size was adequate. Despite this, the results from the study usefully inform clinical practice in this area. Reduced titration of the MAS may have resulted in a lower response rate, thereby reducing the apparent difference in treatment effects. Similarly, the inability to standardize the TSD suction levels and degree of tongue protrusion, which are unable to be measured, may have affected treatment outcome. The randomized crossover design, while an important strength of this study in eliminating between-patient variability, had a relatively short duration. Questionnaires were useful in providing feedback on the patients experience with the devices, but they relied on the accuracy of patient reporting, which may have resulted in responses that minimized or exaggerated the experience of patients. More information may have been obtained if the patients had been able to use each appliance for a longer period prior to the testing phase of the study. The important question of clinical effectiveness was not resolved by our short-term study.

In conclusion, this study showed that 4 weeks of MAS and 4 weeks of TSD can improve the parameters of OSA, including daytime and nocturnal symptoms. Although the findings suggest similar treatment effects of the two appliances in terms of reducing AHI, the higher complete response rate, overall acceptance, and compliance with MAS suggest it is a superior treatment for OSA in the clinical setting. However for subjects who are able to tolerate TSD, or are inappropriate for MAS (e.g., insufficient teeth), this may be a viable treatment option, and further work is required to evaluate the role of TSD in the management of OSA.

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DISCLOSURE STATEMENT

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Aveo Tongue Stabilizing Device For Treatment of Obstructive Sleep Apnea

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Abstract

Introduction: Oral appliances are a simpler alternative to CPAP for the treatment of obstructive sleep apnea (OSA) as they are quiet, portable and don not require a power source.

Aim of the work: The aims of this work were to evaluate the efficacy and complications of Aveo tongue stabilizing device in the treatment of OSA and to determine the predictors of success.

Results: There were significant improvement of symptoms of OSA (snoring, daytime sleepiness, morning headache, nocturnal choking and witnessed apnea) while wearing the device in comparison to before wearing the device (P = 0.002, 0.003, 0.005, 0.025 and 0.046 respectively), The AHI and arousal index were significantly decreased while wearing the device in comparison to without wearing the device (23.67 ± 4.03 vs 9.93 ± 6.52, P < 0.001 and 31.07 ± 4.06 vs 20.67 ± 4.68, P < 0.001 respectively). Success was achieved in(9 cases out of 15) 60%, 40% with complete success and 20% with partial success while 40% showed treatment failure. Side effects of use of TRD were as follow: 80% excessive salivation, 66.67% dry mouth, 60% tongue abrasion and 6% jaw pain. The succeeded cases in comparison to failed cases showed significantly smaller neck circumference, lower BMI, lower AHI, lower % total slept time SaO2 < 90% and predominant supine AHI (P < 0.001, 0.002, 0.001, 0.002and 0.003 respectively)

Conclusion: we can conclude that Aveo TRD was effective in treatment of 60% of mild to moderate OSA and side effects occurred frequently to the extent to prevent 40% of patients to stop use of the device. The predictors of success were cases with low BMI, small neck circumference, low AHI and less hypoxemia and predominant supine AHI.

Introduction:

Although continuous positive airway pressure (CPAP) provides the most widely used method to treat sleep disordered breathing today, it is also the most cumbersome one. Many patients find it unappealing, difficult to tolerate and unacceptable, the only other non invasive alternative which can produce favorable results within a short time is oral appliance (1). Oral appliances are a simpler alternative to CPAP for the treatment of obstructive sleep apnea (OSA) as they are quiet, portable and don not require a power source (2).

In broad terms, oral appliance can be regarded as being either mandibular advancement splint (MAS) or tongue retaing device (TRD). MAS generally attach to the dental arches and mechanically protrude the mandible. TRD use suction pressure to maintain the tongue in a protruded position during sleep. MAS therefore require the patient to have sufficient teeth whereas TRD can be used by edentulous patients (3).

The American Academy of Sleep Medicine recommended the use of oral appliances for mild to moderate OSA or patients with severe OSA who are unable to tolerate CPAP or refuse treatment with CPAP. There is reboust evidence of the efficacy of oral appliances both in regard to improvement of polysomnography (PSG)

indexes as well as modifying the health risk associated with OSA (3).

Aims of the work:

The aims of this work are to evaluate the efficacy and complications of Aveo tongue stabilizing device in the treatment of OSA and to determine the predictors of success.

Subjects and methods:

This prospective study was done in Thoracic Medicine Department, Mansoura University Hospitals in collaboration with Radiology Department, Mansoura Faculty of Medicine and Prosthodontic department Mansoura Faculty of Dentistry in the period from January 2008 to May 2009.

The inclusion criteria of the cases of this study were at least two symptoms of OSA (snoring, fragmented sleep, witnessed apneas, morning headache and daytime sleepiness) and evidence of OSA on PSG (apnea hypopnea index (AHI) ≥ 5/hour), but cases with severe OSA (AHI > 30/hour) were excluded. Other exclusion criteria include bruxism, central apneas, regular use of sedatives, exaggerated gag reflex and standard contraindications for magnetic resonance imaging (MRI) such as cardiac defibrillators and metallic prothesis.

From twenty patients who commenced the trial, 15 patients completed the study (2 patients refused the device and 3 patients dropped during follow up). For the remaining fifteen patients, the following were done:

1) Thorough history taking with stress on symptoms of OSA.
2) Physical examination with stress on neck circumference, body mass index (BMI), and upper airway examination to exclude space occupying lesions in the nose and mouth and dental examination (teeth and gum).
3) Full night PSG(Jaeger sleep screen) for objective diagnosis of OSA and repeated later on after 1 month of acclimatization of the patients on the device for assessment of response to appliance. Positional OSA means >50% of AHI occur in supine position .
4) Consultation with the Prosthodontic Department, Mansoura Faculty of Dentistry, was done for proper insertion of the TRD device intraorally.
   The TRD used in this study was a preformed ,non adjustable appliance. Aveo tongue stabilizing device (Aveo) made by Innovative Health Technology PO Box 17572 Chritchurch, New Zeland.

   It consist of a narrowed isthmus which only extend intraorally to incorporate the incisor teeth or in edentulous patients, the alveolar ridge. This isthmus is joined anteriorly to a bulbous compartment. The tip of the tongue is inserted into the bulbous compartment, which contain vertical supports to hold the tongue in a forward position by negative pressure.
5) Intraoral examination was made to exclude any local inflammatory causes which prevent placement of the device, so thorough scalling and tongue examination was performed and the prosthodontist exclude the patients with parafunctional habits after examination of the existing occlusion. He also learned the patients how to insert and remove the device intraorally and instruct the patient for the way for maintaining the proper oral hygiene measures and hygiene measures of the device. Follow up program for all the

patients was performed during the period of study every week.

6) MRI (Siemens, Symphony 1.5 Tesla) was done on the upper airways with assessment of the shortest retropalatal and retroglossal dimensions (Antero-posterior and lateral) with and without wearing the device while the patients were awake in supine position. A mid saggital slice was done first and from which the shortest retropalatal and retroglossal transaxial slices were chosen for calculation of antero-posterior and lateral dimensions.
7) Response to the device (symptoms of OSA especially Epworth sleepiness scale (ESS) and results of PSG while wearing the device were assessed after 1 month of use of the device. Complete success means reduction of AHI to a level of normal (< 5 events / hour). Partial success means > 50% reduction in AHI but the residual AHI > 5 events / hours. Treatment failure means < 50% reduction in AHI (3).
8) Assessment of complications and compliance were done after 1 month of wearing the device.

Statistics: Data was analyzed using SPSS (Statistical Package for Social Sciences) version 10. Qualitative data were presented as number and percent. Comparison between groups was done by Z-test and Chi-square test. Normally distributed data was presented as mean ± SD. Student t-test was used to compare between two groups. $P < 0.05$ was considered to be statistically significant.

Results:

This prospective study comprised 15 patients with OSA. The mean age was 36 ± 3.3 years, 60% (9 of 15) were males and 40% (6 of 15) were females, the mean BMI was 29.8 ± 1.9 and mean neck circumference was 40.2 ± 2.8 cm.

Table (1): Symptoms of studied cases of OSA without and with use of the oral appliance.

Symptoms	Without oral appliance		With oral appliance		Statistics	
	No	%	No	%	Z	P value
1) Snoring	15	100	5	33.3	3.16	0.002
2) Daytime sleepiness	15	100	6	40	3.0	0.003
3) Morning headache	11	73.3	3	20	2.83	0.005
4) Nocturnal choking	9	60	4	26.7	2.24	0.025
5) Witnessed apnea	8	53.3	4	26.7	2.0	0.046

Table (2): ESS of studied cases of OSA without and With use of oral appliance.

	Mean ± SD	Statistics
ESS without oral appliance	13.33 ± 1.29	t = 10.84
ESS with oral appliance	9.6 ± 1.84	P < 0.001

ESS Epworth sleepiness scale

Table (3): PSG parameters in studied cases of OSA without and with oral appliance.

PSG parameters	Without oral appliance Mean ± SD	With oral appliance Mean ± SD	Statistics
(1) Desaturation index (events/hour)	17.6 ± 2.35	14.1 ± 3.5	t = 10.09 P < 0.001
(2) Average duration SaO2 < 90% (second)	23 ± 3.89	18.67 ± 5.77	t = 6.96 P < 0.001
(3) Minimum SaO2 %	81.47 ± 30.4	85.6 ± 4.05	t = 6.63 P < 0.001
(4) % Total sleep time SaO2 < 90%	2.85 ± 0.82	1.89 ± 0.95	t = 16.42 P < 0.001
(5) AHI (events/hour)	23.67 ± 4.03	9.93 ± 6.52	t = 15.69 P < 0.001
(6) Arousal index (events/hour)	31.07 ± 4.06	20.67 ± 4.68	t = 13.34 P < 0.001
(7) % Total sleep time of snoring	15.76 ± 5.99	4.2 ± 4.14	t = 10.033 P < 0.001

Sao2 Arterial oxygen saturation AHI Apnea hypopnea index

Table (4): MRI of the upper airways of studied cases of OSA without and with oral appliance.

	Without oral appliance Mean ± SD	With oral appliance Mean ± SD	Statistics
Retropalatal			
(a) Anteroposterior dimension (millimeter)	4.53 ± 0.52	6.60 ± 0.51	t = 9.025 P < 0.001
(b) Lateral dimension (mm)	8 ± 0.76	11.1 ± 1.6	t = 16.16 P < 0.001
(c) Anteroposterior / Lateral ratio	0.57 ± 0.10	0.59 ± 0.10	t = 7.485 P < 0.001
Retroglossal			
(a) Anteroposterior dimension (mm)	10.5 ± 0.52	13.7 ± 1.03	t = 14.4 P < 0.001
(b) Lateral dimension (mm)	19.7 ± 0.45	23.7 ± 1.5	t = 11.8 P < 0.001
(c) Anteroposterior / Lateral ratio	0.53 ± 0.02	0.58 ± 0.02	t = 6.537 P < 0.001

Table (5): Outcome of aveo-tongue stabilizing device in patients with OSA.

	No	%
Complete success	6	40
Partial success	3	20
Treatment failure	6	40
Total	15	100

Table (6): predictors of success in studied cases of OSA with oral appliance.

	Success (9) Mean ± SD	Failure (6) Mean ± SD	Statistics
Age	35.67 ± 3.39	36.50 ± 3.51	t = 0.460 P = 0.653
Neck circumference	38.11 ± 1.05	43.33 ± 1.03	t = 9.473 P < 0.001
BMI	29.11 ± 1.36	32.83 ± 2.23	t = 3.869 P = 0.002
ESS	12.78 ± 0.67	14.17 ± 1.60	t = 2.347 P = 0.035
Basal SaO2	90.89 ± 0.93	91.17 ± 0.75	t = 0.609 P = 0.553
% Total sleep time SaO2 < 90%	2.37 ± 0.61	3.57 ± 0.51	t = 3.955 P = 0.002
AHI	20.67 ± 1.73	28.17 ± 0.41	t = 12.481 P < 0.001
Arousal index	30.89 ± 3.48	31.33 ± 5.16	t = 0.200 P = 0.844
% Total sleep time snoring	13.82 ± 7.05	18.17 ± 2.07	t = 1.942 P = 0.081

Table (7): Effect of positional OSA on outcome of oral appliance

	Predominant Side AHI (8)	Predominant supine AHI (7)	Statistics
Success (9)	2 (25%)	7 (100%)	$\chi^2 = 8.750$
Failure (6)	6 (75%)	0 (0%)	P = 0.003

Table (8): Compliance of use of aveo tongue stabilizing device in patients with OSA.

	No	%
Compliant	9	60
Non compliant	6	40
Total	15	100

Table (9): Complications of Aveo tongue stabilizing device in patients with OSA.

	No	%
Excessive salivation	12	80
Oral dryness	10	66.7
Tongue abrasion	9	60
Jaw pain	1	6

Discussion:

Although continuous positive airway pressure (CPAP) provides the most widely used method to treat sleep disordered breathing today, it is also the most combersome one. Many patients find it unappealing, difficult to tolerate and unacceptable, the only other non invasive, alternative which can produce favorable results within a short time is oral appliance (1). The growing literatures regarding the benefits of oral appliances in the treatment of OSA has a growing enthusiasm for their use in clinical practice. There is now an increasing evidence base to support the use of oral appliances in clinical practice (4).

The aims of this work were to evaluate the efficacy and complications of Aveo tongue stabilizing device in the treatment of OSA and to determine the predictors of success.

There were significant improvement of symptoms of OSA (snoring, daytime sleepiness, morning headache, nocturnal choking and witnessed apnea) while wearing the device in comparison to before wearing the device ($P = 0.002$, 0.003, 0.005, 0.025 and 0.046 respectively), and the percentage of total sleep time spent in snoring was significantly decreased with wearing the device compared to before wearing the device ($15.76 \pm 5.99\%$ vs $4.2 \pm 4.14\%$, $P < 0.001$). Also the ESS was significantly decreased from 13.33 ± 1.29 before appliance to 9.6 ± 1.84 after appliance ($P < 0.001$). This was in accordance to schohofer et al (5) who reported on using TRD an improvement of snoring and ESS ($P < 0.05$). Dort and Hussein (6) reported a reduced snoring by more than 70% with the use of TRD. Hoffstein (1) on surveying different investigations found on use of different oral appliances an improvement of snoring by a mean of 45% by using different methods for assessment of snoring (visual analogue scale, number of snores/hour, amount of time spent with loud snoring/hour, number of night/week spent with snoring) also found that ESS dropped from mean of 11.2 to 7.8 which was statistically significant. Dean et al (7) reported that TRD stopped snoring in 33.3% and stopped and reduced it in 55.5% while the ESS was reduced significantly from 8.72 ± 4.52 to 3.78 ± 2.53 ($P = 0.009$). This illustrate that our results and the previously mentioned studies documented the improvement of OSA symptoms with the use of TRD.

The AHI and arousal index were significantly decreased while wearing the device in comparison to without wearing the device (23.67 ± 4.03 vs 9.93 ± 6.52, $P < 0.001$ and 31.07 ± 4.06 vs 20.67 ± 4.68, $P < 0.001$ respectively). This was in accordance to compilation of data from four peer reviewed studies (57 patients using TRD) which showed a mean decrease of AHI from 44 to 22 (Cartwright and Samuelson (8), Cartwright (9), Cartwright et al (10), and Cartwright et al (11). Ferguson et al (12) on use of TRD reported significant decrease in AHI from 45/hour to 19/hour ($P < 0.001$). Ferguson et al (4) on reviewing ten studies of different oral appliances reported a reduction of baseline by 50%. Dean et al. (7) with the use of Aveo TRD reported that the AHI decreased from 28.66 ± 4.39 to 13.01 ± 2.65 $P = 0.002$ and the arousal index decreased from 34.6 ± 4.04 to 21.93 ± 2.47 $P = 0.003$, while Barthlen et al (13) reported that AHI do not change significantly from 50.3 ± 18.9 at baseline to 43.5 ± 32.5 with the device ($P = 0.64$). This insignificant result can be explained by small number of studied cases (only 5 patients). Also Kingshott et al (14) reported a non

significant decrease of AHI from 20 ± 17 to 15 ± 13 P = 0.06 while the arousal index was significantly decreased from 34 ± 16 to 22 ± 14 P = 0.004. The explanation here for this non significant AHI also was the small number of studied cases (6 patients).

The parameters of SaO2 in our study showed significant improvement with the use of the device in comparison without use of the device. For desaturation index was 17.6 ± 2.35 vs 14.1 ± 3.5 events/hour P = 0.001, for average duration of SaO2 < 90% was 23 ± 3.89 seconds vs 18.67 ± 5.77 seconds P < 0.001, for % total sleep time (TST) SaO2 < 90% 2.85 ± 0.82% vs 1.89 ± 0.95% P < 0.001, and for minimum SaO2 was 81.47% ± 30.4 vs 85.6% ± 4.05 P < 0.001. This was in accordance to Higurashi et al (15) who reported significant increase in minimum SaO2 P < 0.05 and significant decrease % of TST spent with SaO2 < 90% P < 0.05, also in accordance to Deane et al (7) who reported that the minimum SaO2 was significantly increased from 83.3 ± 1.54% to 88 ± 1.24 %P = 0.003.Our results and the previously mentioned studies documented improvement of objective parameters of OSA (AHI, Arousal index, Desaturation indexes) with the use of TRD.

The antiroposterior (AP) and lateral (L) dimensions in the retropalatal and retroglossal areas were significantly increased with the wearing of the device in comparison to without wearing of the device. They were in retropalatal area 4.53 ± 0.52 mm vs 5.6 ± 0.51 mm (P < 0.001) for AP dimension and 8 ± 0.76 vs 12.1 ± 1.6 mm (P < 0.001) for (L) dimension, and in retroglossal area, 10.5 ± 0.52 mm vs 13.7 ± 1.03 mm P < 0.001 for (AP) dimension and 19.7 ± 0.45 mm vs 23.7 ± 1.5 mm (P < 0.001) for (L) dimension. This was in accordance to Ferguson et al (12) who reported that maximal protrusion of the tongue significantly increased the cross sectional area of the oropharynx and velopharynx P < 0.001. A lesser degree of the tongue protrusion also significantly increase the oropharynx cross sectional area P < 0.05 but not the velopharynx cross sectional area. Also our results are in accordance to Deane et al (7) who reported that the (AP) dimension significantly increased with the use of Aveo-TRD in the oropharynx (10.87 ± 1.12 mm vs 13.24 ± 0.83 mm P = 0.033) and also significantly increased the (L) dimension in velopharynx and oropharynx (15.43 ± 2.26 mm vs 20.05 ± 2.17 mm P = 0.044 and 19.85 ± 1.58 mm vs 24.57 ± 1.88 mm P = 0.034 while no significant differences of the (AP) dimension in the velopharnx (9.01 ± 1.08 mm vs 9.95 ± 1.02 mm P = 0.26). The difference between our result and that of Deane et al (7) can be explained by the difference in the degree of protrusion of the tongue during imaging which will be significant on maximal protrusion as in study of Ferguson et al (12). Our results and the previous studies document the increase in AP and L dimensions of velopharynx and oropharynx which illustrate the mechanism by which TRD improve OSA. Another possible mechanism is the change in muscle tone of pharyngeal muscles which need further investigation.

In our study, the AP/L ratio increased while wearing the device (from 0.57 to 0.59 in the palatopharyngeal area and from 0.53 to 0.58 in the glossopharyngeal area.this was statistically significant (p<0.001 for both). This was in accordance to Ferguson et al (12) who reported that AP/L diameter ratio increased with maximal tongue protrusion in oropharynx and velopharynx P < 0.001. The tongue protrusion resulted in a change in shape of the upper airway

from laterally oriented ellipse to a some what more circular contour. This change in shape was achieved through ventral displacement of the epiglottis, tongue and soft palate.

In our study, success was achieved in 9 cases out of 15 (60%), 40% (6 out of 15) with complete success and 20%(3 out of 15) with partial success while 40% (6 out of 15) showed treatment failure. Schonhofer et al (16) on use of snore Ex oral appliance reported significant decrease in AHI in compliant patients to the apparatus (6 patients) (32.7 ± 11.5 vs 16.7 ± 4.3, $P < 0.05$). Moses and Alvarez (17) reported that TRD make a comeback and prove their validity through a plethora of scientific researches. Hoffstein (1) on surveying 73 studies with a total of 2729 patients using different oral appliances achieved complete success in 54% and partial success in 21%. Yow (18) reported overall success rate of oral appliances in mild to moderate OSA to be in the range 57 – 81%. Deane et al. (7) on using Aveo TRD reported success rate of 6 out of 14 (42.81%), 28.5% for complete success and 14.3% for partial success in cases with mild to moderate OSA, and 75% (3 out of 4) with partial success in cases with severe OSA. The total success rate was 50% (9 out of 14). Our results documented that TRD achieved success in the lower range reported by Hoffstein (1) and Yow (18) by using different oral appliances mostly mandibular advancement device (MAD). This was in accordance to Deane et al (7) who reported a higher success rate with the use of MAD in comparison to Aveo TRD (67.7% vs 50%) but with no significant difference ($p=0.38$). On the reverse of our results and previous studies, Barthlen et al (13) reported slight decrease in AHI from 50.3 ± 18.9 to 43.5 ± 32.5) and Kingshott et al (14) reported a non significant trend for reduction in AHI with use of TRD. The mean reduction in AHI was 11/hour slept ± 10 SD. The non significant decrease in the AHI in the previous two studies can be explained by small number of studied cases (5 cases in the first study and 6 cases in the second study).

In our study, the succeeded cases in comparison to failed cases showed significantly smaller neck circumference, lower BMI, lower AHI, lower % total slept time $SaO2 < 90\%$ and predominant supine AHI ($P < 0.001$, 0.002, 0.001, 0.002and 0.003 respectively). These were in accordance to Ferguson et al (4), Chan et al (3), Yow (18) who reported that success of oral appliance occurred more in cases with lower AHI, lower BMI, smaller neck circumference and supine dependent OSA. These factors can be used in the future as predictors of success of use of Aveo TRD.

In our study, side effects of use of TRD were as follow: 80% excessive salivation, 66.67% dry mouth, 60% tongue abrasion and 6% jaw pain. These side effects leads to non compliance (discontinuation of use of the device) in 6 cases out of 15 (40%). This was in accordance to Ferguson et al. (4) who reported that tongue pain prevented the use of TRD in 3 out of 8 cases (37.5%, also was in accordance to Deane et al. (7) who reported that TRD side effects were as follow: excessive salivation in 85%, dryness of mouth in 68%, soft tissue irritation in 61.1%, jaw discomfort in 11.5%. These side effects prevented 50% of patients from using TRD.

The limitations of this study include that the MRI imaging of the upper airway of awake patients which differ from the physiologic state of sleep, relatively small number of studied cases and short duration of follow up. So further studies are needed to support the results of our study.

From this study, we can conclude that Aveo TRD was effective in treatment of 60% of mild to moderate OSA and side effects occurred frequently to the extent to prevent 40% of patients to stop use of the device. The predictors of success were cases with low BMI, small neck circumference, low AHI and less hypoxemia and predominant supine AHI.

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ORIGINAL ARTICLE

The Efficacy of a Novel Tongue-Stabilizing Device on Polysomnographic Variables in Sleep-Disordered Breathing: A Pilot Study

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ABSTRACT

The polysomnographic efficacy of a novel tongue-stabilizing device (TSD) in the treatment of snoring and sleep-disordered breathing (SDB) was evaluated in this pilot study. Six current users of the TSD with SDB underwent polysomnography with and without the TSD in situ in a randomized crossover design. The TSD significantly lowered the frequency of snores per hour slept (61- to 70-dB range) (no TSD: mean = 41/h slept ± 52 SD; TSD: 8/h slept ± 16 SD; P = 0.046) but did not alter snoring in the other decibel ranges (all Ps > 0.1). Trends were found for reductions in the frequency of apneas plus hypopneas (no TSD: 26/h slept ± 17/h slept; TSD: 15/h slept ± 13; P = 0.06) and oxygen desaturations of 4% or more (no TSD: 10/h slept ± 10; TSD: 5/h slept ± 5; P = 0.09). Significant improvements in microarousal frequency with the TSD were found (no TSD: 34/h slept ± 16; TSD: 22/h slept ± 14; P = 0.004). Significant reductions in percentage of Stage 1 sleep with the TSD were also demonstrated (no TSD: 10 ± 3%; TSD: 8 ± 2%; P = 0.03). The results of this small pilot study indicate that the TSD may be effective in reducing snoring severity and microarousals, with favorable trends for reducing SDB severity in selected individuals. Additional larger prospective studies are required to identify suitable candidates for TSD use in the treatment of snoring and SDB.

KEYWORDS: Oral appliances, tongue retainers, sleep-disordered breathing, snoring

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Sleep-disordered breathing (SDB) ranges from snoring to severe obstructive sleep apnea (OSA).[1] Continuous positive airway pressure (CPAP) is the current treatment of choice for moderate to severe OSA.[2,3] Mandibular advancement splints have been used as an alternative first-line therapy for the management of SDB, in particular for snoring and mild sleep apnea. These intraoral devices hold the mandible in a forward position, thus potentially increasing upper airway dimensions. [4–6]

Less attention has been focused on a second type of oral appliance devised in the 1980s: tongue-retaining devices (TRDs).[7] These devices contain a plastic bulb into which the anterior part of the tongue is positioned. The bulb is depressed to create a negative suction pressure and hold the tongue in a forward position. TRDs have been shown to significantly reduce the frequency of breathing pauses and improve sleep quality.[4,7,8] The tongue protrusion created by a TRD increases oropharyngeal, hypopharyngeal, and velopharyngeal cross-sectional areas of the upper airway during awake states.[9] TRDs have also been shown to affect genioglossus muscle activity in a different manner in awake sleep apneics compared with controls.[10] Therefore, it is hypothesized that tongue protrusion alters the shape of the upper airway and is important in alleviating impaired upper airway function.

The tongue-stabilizing device (TSD) was developed by Christopher J. Robertson and manufactured in the United States (Great Lakes Orthodontics, Ltd., Tonawanda, New York) (Figs. 1 and 2). Based on the bulbous compartment of the TRD, this novel oral appliance incorporates a narrowed isthmus joined to the anterior bulbous compartment. The tip of the tongue is inserted into the bulbous compartment, which contains vertical external supports to hold the tongue in a forward position by negative pressure. TRDs incorporate some form of occlusal stop or grooving over the dentition and in doing so usually require the taking of dental impressions. In contrast to the TRD, the TSD only extends intraorally to incorporate the incisor teeth or, in edentulous patients, the alveolar ridge. The TSD is a nonadjustable universal device that is available in four different sizes. In addition, the TSD allows for oral breathing, has no moving parts, and is small and simple to use. As such, it was designed as an inexpensive "off-the-shelf" product for health professionals involved in the treatment of snoring and SDB.

Figure 1 Tongue-stabilizing device: (A) lateral view; (B) superior view; (C) anterior view.

Currently, the TSD is prescribed for the treatment of self- or partner-reported snoring. Treatment success is based on subjective reduction in snoring and daytime dysfunction. The objective effi-

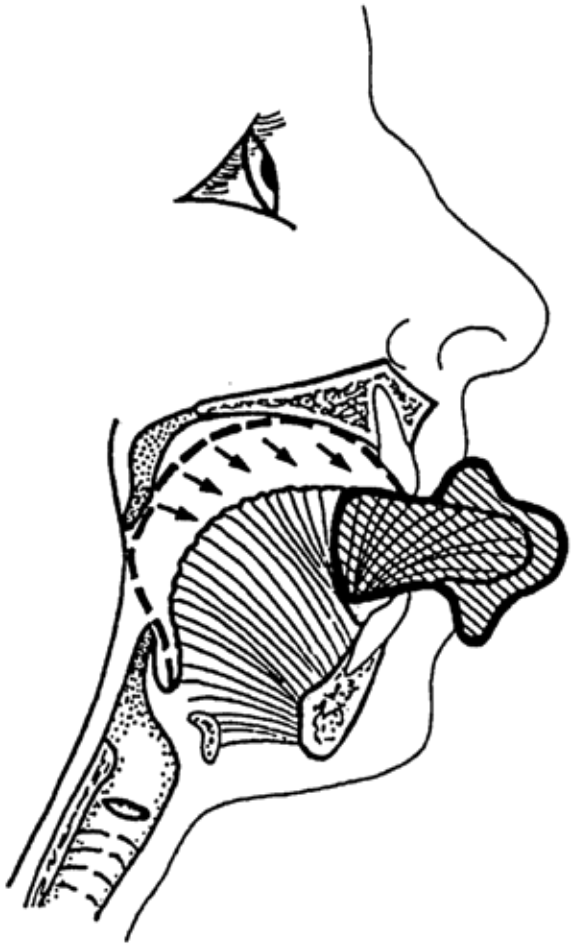

Figure 2 Tongue-stabilizing device in situ.

cacy of the TSD as a therapy for SDB is not known. The aim of the current pilot investigation was to examine the effect of the TSD on polysomnographic variables in patients with mild SDB who were already using the TSD.

METHODS

Patients

Suitable study patients had been medically referred from Sleep or Ear, Nose, and Throat Clinics to the University of Otago Orthodontic Outpatient Clinic for the treatment of snoring and had been fitted with TSDs. Inclusion criteria were as follows: current TSD users (> 3 h/night, self-reported), use of TSD for more than 2 months, and willingness to stop using TSD for one night. Exclusion criteria were self-reported symptoms of OSA, which would constitute a referral to the Sleep Laboratory for polysomnography; taking medication known to affect muscle activity; previous upper airway surgery; and ongoing treatment for SDB.

Eight patients had been issued with the TSD and fulfilled the study criteria. Six male patients (mean age: 51 years ± 4 SD; mean body mass index: 30 kg/m^2 ± 3) agreed to participate. The remaining two patients were unable to take part because of family and work commitments.

The Otago Ethics Committee approved the study, and each study participant provided written informed consent. The TSD has Food and Drug Administration approval for the treatment of snoring (FDA No. K993381).

Study Design

The pilot study was a single-center efficacy trial. Each patient attended the Sleep Laboratory on two consecutive nights: one night with the TSD in situ and one night without the TSD in situ. The order was randomized.

Overnight Polysomnography

On both study nights, patients attended the Sleep Laboratory for full diagnostic polysomnography.[11] Before their arrival, patients were instructed to abstain from caffeinated beverages and alcohol for at least 4 hours. Sleep was monitored by electroencephalography (EEG; C3-A2 and O2-A1), electrooculography, and submental electromyography (EMG). Thoracic and abdominal respiratory movements were measured by inductance plethysmography and arterial oxygen saturation using pulse oximetry. Electrocardiogram, body position, and right and left leg movements were also monitored. In

addition, an integrated sound meter (NL-05, Rion Co., Ltd., Tokyo, Japan) monitored sound levels. The calibrated sound meter was situated at the side of the bed; the microphone was located 4 cm out from the wall at the head of the bed and 20 cm above the pillow. All signals were recorded onto a computerized system (Compumedics S, Victoria, Australia) using a 16-channel polygraph configuration. On the study night with the TSD in situ, patients were instructed to use their device all night.

Off-Line Analysis Sleep stages were manually scored using standard Rechtschaffen and Kales scoring guidelines.[12] Sleep stage values were expressed as a percentage of sleep period time. An apnea episode was defined as a complete cessation of airflow for a minimum of 10 seconds and hypopnea as a 50% reduction in thoracoabdominal movement for a minimum of 10 seconds.[13] The total number of respiratory events was divided by total sleep time to give the apnea–hypopnea index (AHI) per hours slept. Microarousals were scored using the definition of a return to alpha or theta waves on the EEG for a minimum of 3 seconds during non-rapid eye movement sleep, with the addition of a concurrent minimum 3-second rise in submental EMG tone during rapid eye movement sleep.[14] Both spontaneous and respiratory event-related arousals were included in the microarousal frequency. Oxygen desaturations of 4% or more of baseline were calculated from each overnight study using an automatic desaturation detection algorithm (Compumedics S) and divided by total sleep time to give a desaturation index per hour slept. The snore parameters were as follows: The background baseline value was set at 40 dB in each bedroom, a minimum deviation of 5dB from the sound baseline was required before a snore was detected, and the minimum time between snores was 1 second. Each peak snoring sound was then automatically counted and placed into a range of decibel bins using an automated program (Compumedics S) and divided by total sleep time to give a snore index for each decibel range. Each record was anonymous so that the polysomnographer was unaware of whether the TSD was in situ or not.

Statistical Analyses

Paired data were analyzed using mixed two-way analysis of variance for repeated measures, with treatment as a within-subject factor and treatment order as a between-subject factor. Order effects were seen for percentage of Stage 2 sleep and percentage of slow wave sleep. These data were, therefore, analyzed as suggested by Hills and Armitage[15] using an unpaired *t* test on first-limb data only. Snore indexes in the ranges of 51 to 60 dB and 61 to 70 dB displayed substantial heterogeneity of variance and were compared using Wilcoxon rank-sum tests for paired differences. A probability value of less than 0.05 was accepted as statistically significant. All data were analyzed using SPSS version 10 for Windows.[16]

RESULTS

Participants

All participants reported wearing their TSD for the complete duration of the study night.

Efficacy Measures

Snoring Use of the TSD significantly decreased the snore frequency in the 61- to 70-dB range ($P = 0.046$). However, no significant improvements in snoring levels were seen in the other decibel ranges or in the overall frequency of snores per hour slept with the TSD in situ (Table 1; Fig. 3).

AHI A nonsignificant trend was seen for a reduction in AHI with the TSD (Table 2; Fig. 4). The mean reduction in the AHI with the TSD in situ was 11/h slept $\pm$ 10 SD.

Table 1 Treatment Differences in Sound Levels (N = 6)

Snoring Index	Without TSD†	With TSD†	P
45–50 dB	90 ± 52	115 ± 4	0.16
51–60 dB	196 ± 208	100 ± 55	0.17
61–70 dB	41 ± 52	8 ± 16	0.046
>70 dB	1.3 ± 3	0.7 ± 1	0.35
Total snore peaks	329 ± 282	223 ± 106	0.31

TSD, tongue-stabilizing device.
†Values represent mean ± standard deviation.

Oxygen Desaturations There was a nonsignificant trend for a reduction in the frequency of oxygen desaturations of 4% or more when the TSD was in situ (see Table 2).

Arousal Frequency A significant decrease was noted in the arousal frequency with the TSD in situ (see Table 2; Fig. 5). The mean reduction in the arousal frequency with the TSD in situ was 12/h slept ± 5 SD.

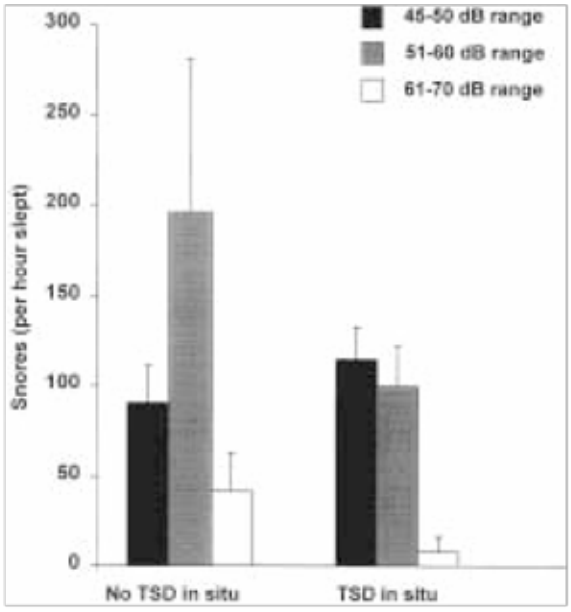

Figure 3 Comparison of snoring levels with and without the tongue-stabilizing device in situ.

Sleep Stages Use of the TSD significantly decreased the percentage of Stage 1 sleep (P = 0.03); however, the TSD had no significant effect on any of the other sleep stages, including stage wake (see Table 2). Total sleep time was not significantly different (P = 0.7) between the two study nights.

Treatment Outcome Of the six participants, three were recommended by the respiratory and sleep physician (D. Robin Taylor) to continue using the TSD as first-line treatment for SDB or snoring. The three remaining patients were recommended CPAP therapy, a mandibular advancement splint, and conservative therapy (alcohol avoidance and sleep position training), respectively, as first-line therapy.

DISCUSSION

This study examined the effect of a novel TSD on polysomnographic variables in the treatment of SDB. In this pilot study, the TSD significantly reduced snoring and sleep fragmentation. The TSD did not significantly lower the AHI or frequency of oxygen desaturations of 4% or more, although trends were found. Findings indicate that the TSD may be an effective therapy in selected individuals with SDB and snoring. Further study is required to determine whether these statistically significant improvements correspond with any clinical benefit and which factors can predict TSD treatment success.

A significant reduction in snoring in the 61- to 70-dB range was found in the current study, in agreement with subjective snoring reports from a previous study using a TRD.[17] Significant reductions in objective snoring sounds have been demonstrated in an efficacy study using a mandibular advancement splint.[18] The TSD was not as effective as the mandibular advancement splint in reducing snoring in our population sample; no significant changes in the other decibel ranges were seen. One possible explanation for the lack of a greater reduction in snoring

Table 2 Treatment Differences in Nocturnal Sleep and Respiratory Variables (N = 6)

Variable	Without TSD*	With TSD*	P
Apnea-hypopnea index†	26 ± 17	15 ± 13	0.06
≥4% oxygen desaturations†	10 ± 10	5 ± 5	0.09
Arousal frequency†	34 ± 16	22 ± 14	0.004
Total sleep time (minutes)	400 ± 55	410 ± 70	0.72
% Awake	15 ± 6	14 ± 5	0.32
% Stage 1 sleep	10 ± 3	8 ± 2	0.03
% Stage 2 sleep	48 ± 4	43 ± 4	0.15
% Slow wave sleep	11 ± 1	15 ± 5	0.17
% REM sleep	18 ± 6	20 ± 5	0.16

TSD, tongue-stabilizing device; REM, rapid eye movement.
*Values represent mean ± standard deviation.
†Per hour slept.

sounds in our study is that patients only snored intermittently; the snoring was frequently interspersed with hypopneas and occasional apneas. It is possible that the TSD reduced the AHI and replaced the silent airway obstruction with partial airway narrowing, thus increasing snoring sound.

Early studies demonstrated significant reductions in the apnea index with a TRD but were performed before the recognition of hypopneas.[7,19] A later study using a TRD did find significant improvements in AHI with a TRD in situ.[8] The current study demonstrated similar improvements in AHI with the TSD, although significance in our smaller sample was not reached. Cartwright[19] also found that patients with a higher AHI in the supine position responded well to a TRD compared with those with no positional component. Although body position was measured in the current study,

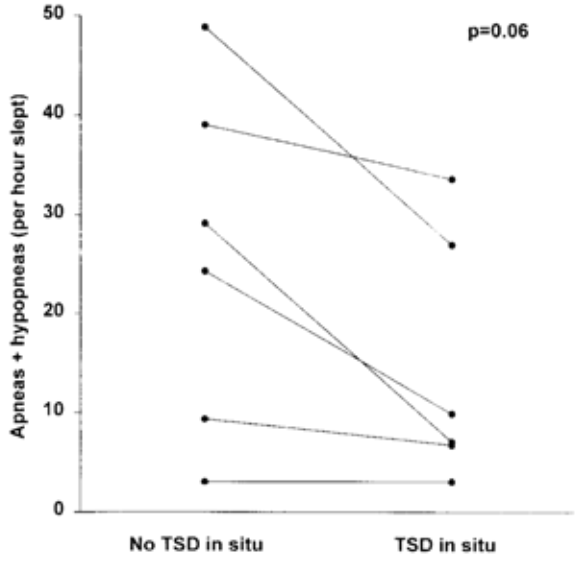

Figure 4 A comparison of the apnea–hypopnea frequency with and without the tongue-stabilizing device in situ.

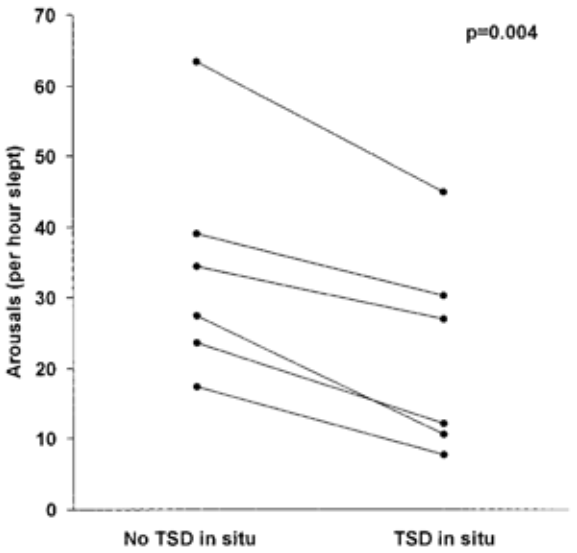

Figure 5 A comparison of the nocturnal arousal frequency with and without the tongue-stabilizing device in situ.

because of the small sample size, subdividing patients into positional and nonpositional SDB was not undertaken. Cartwright[19] also found a significant improvement in the minimum oxygen saturation with a TRD in place. A trend for a reduction in the frequency of oxygen desaturations of 4% or more with the TSD was found in the current study. The greater respiratory treatment success of a TRD could be attributable to the larger sample sizes and greater disease severity studied by Cartwright and Samelson.[7,19] However, it is worth noting that, although TRD studies have demonstrated significant reductions in apnea frequency, the on-treatment apnea indexes remain clinically high for these two studies 22.7 and 32.9/h slept, respectively).[7,19]

The current study found a significant improvement in the arousal frequency with the TSD. Early efficacy studies[7,19] of a TRD were performed before the routine scoring of microarousals; therefore, direct study comparisons cannot be made. However, in agreement with TRD studies,[7,19] the TSD significantly reduced the percentage of Stage 1 sleep. These results indicate that the TSD may reduce the sleep fragmentation associated with SDB.

Limitations to the current study include study power and study design. First, this is a pilot study with a limited sample size. The trends might have been statistically significant with a larger sample size. (Based on our data, if the effect we measured is the true effect, then 23 individuals would be required to detect a significant reduction in AHI and arousal frequency [at $P < 0.05$] with a power of 80%.) Second, the study design has its limitations. Participants were all current users of the TSD who stopped using their devices for one night of polysomnography for the study. This night acted as a "diagnostic" nontreatment night. However, the TSD had been worn consistently for at least 2 months before. Therefore, treatment carryover effects of prior TSD use may have reduced potentially significant differences with and without the TSD in situ. One night without treatment is unlikely to be sufficient to allow the return of upper airway edema. Third, the patients recruited were highly selected; thus, patient acceptability and subjective outcomes were not assessed in the current pilot. Fourth, the sample studied had a wide range of SDB severity. All were self-reported snorers without symptoms of sleep apnea. Yet results demonstrated that four of the six participants had a diagnostic AHI of more than 20/h slept. This highlights the importance of validated questionnaires, screening tools, or prior polysomnography to rule out moderate to severe OSA before fitting an orthodontic device. However, the primary purpose of this pilot was to assess the effect of the TSD on polysomnographic variables rather than predicting disease severity in nonsymptomatic snorers.

The results of this pilot study indicate that the TSD may be an effective therapy in selected individuals with snoring and SDB. Further work on the efficacy and acceptability of the device is required to identify suitable candidates for this simple form of treatment. In addition, the role of the TSD as an alternative, adjunct, or temporary therapy for snoring and SDB needs to be determined.

FUNDING

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FINANCIAL DISCLOSURE

Christopher J. Robertson developed the TSD and has a small commercial interest.

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Tongue Related Papers

Return of the TRD

Commentary on Lazard D, et al. The tongue-retaining device: Efficacy and side effects in obstructive sleep apnea. J Clin Sleep Med 2009;5:431-438.

Rosalind Cartwright, Ph.D.

Rush University Medical Center, Chicago, IL

Journal of Clinical Sleep Medicine, Vol.5, No. 5, 2009

The Origin of Pharyngeal Obstruction during Sleep

Laurence I. Barsh, M.M.D.

Sleep And Breathing, Vol. 3, Number 1, 1999

The Great Leap Forward: the anatomic basis for the acquisition of speech and obstructive sleep apnea

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Sleep Medicine 4 (2003) 185–194

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COMMENTARY

Return of the TRD

Commentary on Lazard D, et al. The tongue-retaining device: Efficacy and side effects in obstructive sleep apnea. J Clin Sleep Med 2009;5:431-438.

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The current emphasis on health care reform in the US encourages the choice of treatment based on evidence of best outcome. Given this thrust, it is good to have the additional data provided in this article to help guide the decision of appropriate therapy for obstructive sleep apnea (OSA).

When the research literature on the efficacy of oral appliances (OA) for the control of OSA was reviewed recently[1] by a committee appointed by the Standards of Practice Committee of the American Academy of Sleep Medicine, the tongue-retaining device (TRD) was tested in very few of the published studies. The literature surveyed, which covered the years 1995 to 2004, found that mandibular advancement devices (MADs) were overwhelmingly the choice of OA being tested. Within this class of OA, there are many differing features, but all work on the same principle—to advance the mandible and thus create more room mechanically in the posterior airway. The TRD, on the other hand, holds the tongue forward by suction, preventing the flaccid tongue from retrolapsing with inspiration and so blocking the airway. Some studies in that review compared the tolerance and effectiveness of an OA to that of the most frequently prescribed treatment, nasal continuous positive airway pressure (CPAP), in cross-over designs. The justification of having an OA as an option to CPAP is some patients' refusal to accept CPAP or their failure to use it enough nights or hours to be effective. Studies in which patients were tested on both an OA and CPAP report that the OA is less effective but better tolerated and preferred by patients when given the choice.[2]

The study by Lazard et al.[3] has much to commend it; it included a large number of patients, more than most studies using a TRD (55 had an initial diagnostic polysomnography study before using the TRD and a second with this device in place). The follow-up period, although variable, is also longer (1 to 91 months, median = 4) than in many studies. Compliance was checked only by a phone interview after 5 years. The data analysis is careful, and the article is well written. Because this study did not involve a comparison test with another type of OA or with CPAP for the same patients, the authors compare their findings to those reported in other studies. The authors conclude that the efficacy of the TRD based on control of apnea was similar to that reported in studies using a MAD.

However, the data from this study are not strictly comparable with others involving either a MAD or TRD, as they excluded patients whose initial polysomnogram identified their apnea to be "positional." These patients were withdrawn from this study and treated to avoid the supine sleep position. Because positionality has been established to be a strong predictor of TRD efficacy,[4] this sample, as the authors admit, is biased. In fact, because they did not enroll the patients most likely to succeed, it is biased against the TRD having an equal or better outcome than has been reported in studies in which the sample was more inclusive. The sample of 55 consisted of patients with severe OSA who had failed treatment with CPAP and some for whom position training was not effective. Their initial assessment of apnea severity is not specified, but, since they failed position training, they are less likely to be successful with a TRD. The remaining patients with mild or moderate OSA had a TRD as a first treatment.

Given the development of good predictors of effectiveness of the TRD, (apnea severity, positionality, and nasal patency), and endorsement by the Standards of Practice report for mild and moderate OSA, why has the TRD not had more use? I suggest one reason is the dominance of sleep clinicians trained in pulmonary medicine who are more familiar and comfortable with CPAP as a treatment choice in spite of its poorer adherence in those whose apnea is mild or moderate.[1] The authors suggest a different reason the TRD is less popular than the MADs—its "esthetic" appearance. On this criterion, it beats CPAP hands down. I believe that, at least in the US, another reason MADs are preferred over a TRD may be related to billable hours. If the sleep clinician refers the patient to a dentist for an OA, they may choose to fit a MAD because it is more labor intensive, involving many more appointments to fit and adjust it. Some also do additional expensive testing, such as videoendoscopy, cephalometrics, and at-home sleep studies. The TRD is a simple 1-piece device that is usually fitted in one appointment. It does not have the problem of a shift in bite, which has been noted in some with the long-term use of a MAD.[1] The TRD is similar in effectiveness to other OA, and, because patients prefer it over

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CPAP[1] and so use it more often and for more hours, it meets the best practice test.

There is general agreement that CPAP should be the treatment of choice for those severe cases (apnea-hypopnea index > 40), but these patients should also be trained to avoid supine sleep, lose weight, stop smoking, and exercise.[5] When these good health habits have brought down their apnea symptoms, but on retesting the patient is still mildly or moderately apneic and/or snoring and sleepy, they can then turn in their CPAP for a TRD.

DISCLOSURE STATEMENT

Dr. Cartwright has indicated no financial conflicts of interest.

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SLEEP AND BREATHING—VOL. 3, NO. 1, 1999

REVIEW ARTICLE

The Origin of Pharyngeal Obstruction during Sleep

LAURENCE I. BARSH, D.M.D.

ABSTRACT: *This paper traces the development of the adult human pharynx through evolution, comparative anatomy, and development from infant to adult. Based on phylogeny and otogeny, an hypothesis for the occurrence of obstructive sleep apnea in the mature human is presented.*

KEYWORDS: obstructive sleep apnea, oropharynx, klinorynchy, evolution, pharynx

Obstructive sleep apnea (OSA) is characterized by repeated pharyngeal obstructions during sleep. The obstructions occur in the velopharyngeal, orophayngeal, and hypopharyngeal regions of the human pharynx. Man is the only animal to suffer from OSA although, arguably, the English bulldog also suffers from a form of sleep disordered breathing.*

What is it that is unique to the human pharynx that predisposes it to collapse during sleep? To answer this question one must investigate the evolution, comparative anatomy and development of the pharyngeal area.

Laitman[1] stated

> The acquisition and processing of oxygen and its byproducts is the primary mission of any air-breathing vertebrate. Chewing, walking, reproducing, thinking are all fine, but first one has to breathe. Anthropologists seem to forget this; evolution never does.

However, despite the importance of respiration to sustaining life, when one considers the muscles of the pharyngeal region in man, it becomes apparent that not one muscle has as its *primary* function dilation of the pharynx. The muscles commonly thought of as the pharyngeal dilator muscles are listed in Figure 2.

What could be the reason that a function so necessary to the life of man as breathing, while awake and asleep, does not have even one muscle dedicated to maintenance of patency of the upper airway? Could it be that pharyngeal dilation for respiration is not necessary in other mammals and was not necessary in the evolutionary development of man? To answer this question, one has to consider the function of the structures of the pharyngeal airway and compare the differences between other mammals and man.

Negus[2] performed postmortem dissections on many types of mammals and found that the epiglottis passes up behind the soft palate to guide the locking of the larynx directly into the nasopharynx. This provides a direct air channel from the external nares through the nasal cavities, nasopharynx, larynx, and trachea into the lungs. Food passes on either side of the interlocked larynx and nasopharynx into the esophagus without interfering with the patent airway. He concluded that the function of the epiglottis in mammals was to subserve the sense of smell by allowing the individual to breathe and eat at the same time. Further in all quadrupeds, such as the horse (Fig. 3), the tongue is located entirely within the oral cavity. (Even in the English bulldog the uvula and epiglottis are interlocked—see Fig. 1) Crelin[3] states that

> After an extensive survey of the literature and dissecting numerous specimens, a general pattern of vocal tract anatomy in the air-breathing vertebrates emerged. Except in the mature human, the tongue is located entirely within the oral cavity or mouth.

It would appear when analyzing air-breathing vertebrates other than the adult human, those with an interlocking epiglottis and uvula, with a straight airway and with a tongue totally housed within the oral cavity, muscles for pharyngeal dilation may be totally unnecessary

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*Hendricks et al[1] have stated that the English bulldog is "characterized by an abnormal upper airway anatomy, with enlargement of the soft palate and narrowing of the oropharynx." Despite the tendency for this breed to suffer sleep-disordered breathing and O_2 desaturation, the pharyngeal airway is unlike that of the adult human. It is, however, similar to the human infant and all nonbrachycephalic animals in that the tongue is contained totally within the oral cavity and, therefore, an oropharynx does not exist (Fig. 1). The development of an oropharynx, as shall be demonstrated in this article, is unique to the mature human. Because of this, the English bulldog cannot be considered an animal model of sleep-disordered breathing from which an exact correlation to adult human obstructive sleep apnea can be extrapolated. However, because of the anatomical similarities of the bulldog pharynx to the infant human, that is, the presence of an interlocking uvula and epiglottis, it is plausible that this animal might represent a model from which to study infantile obstructive sleep apnea and Sudden Infant Death Syndrome.

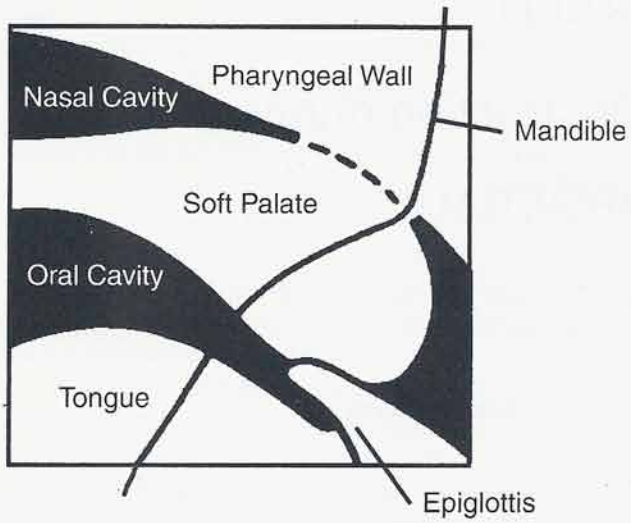

FIG. 1. The airway of the bulldog is extremely narrow in oral cavity and nearly obliterated in nasal cavity by the large soft palate. Furthermore, soft palate extends further caudally, overlapping epiglottis by almost 1 cm. After Hendricks et al. (4).

to maintain patency of the airway. In these animals, the oropharynx does not exist.

One other factor plays a crucial role in the development of obstructive sleep apnea in the human. The anatomy of the human newborn and very young infants (Fig. 4) closely approximates the anatomy of the upper respiratory tract of primates in particular and mammals in general.[5] The close approximation and locking of the uvula and epiglottis allows for the simultaneous suckling of milk and breathing. At an early stage in the ontogenetic development of the human (approximately 18 months), the laryngeal complex migrates from its original subcranial position to lie opposite the fifth cervical vertebra. However, the epiglottis does not undergo any significant morphological change as a result of the relocation of the larynx. This leads to the fact that while in all other animals and the postpartum human infant the epiglottis interdigitates with the soft palate, in the developing human it is increasingly unable to do so. As the interdigitation of these structures effectively resulted in discrete pathways for respiration and deglutition, the development of specific musculature to maintain patency of the pharynx was unnecessary. In the mature human, however, the anterior wall of the respiratory tube is breached throughout the extended length of the newly developed oropharynx. The development of this wide, soft-walled oropharyngeal structure has some advantages in that it provides a resonating chamber in which format frequencies (at the basis of human speech) can be generated,[6] but also provides the opportunity for sleep-induced collapse.

The adult human pharynx differs substantially from the human infant and other air-breathing mammals. As an individual evolutionarily assumes an erect posture, changes occur in the relationship between the position of the foramen magnum at the base of the skull and the spinal column as well as between the braincase (neurocranium) and the facial skeleton (splanchnocranium). The human facial skeleton lies below the frontal region of the braincase rather than in front of it, as in most quadrupedal animals. The facial migration that results in this positioning of the splanchnocranium, known as klinorynchy, constricts the available subcranial space to the extent that a change in pharyngeal and laryngeal morphology is necessitated.[6] The process of klinorynchy can be summarized in Figure 5.

Crelin[7] writes that

> In the present day apes, I found that the tongue occupies the entire oral cavity with the jaws closed, and its length is directly related to the length of the oral cavity. Thus, the

MUSCLE	ACTION
Digastricus	Elevates hyoid; depresses mandible
Genioglossus	Protrudes tongue (inf. fibers); depresses tongue (mid. fibers)
Geniohyoid	Elevates hyoid; depresses mandible
Levator Veli Palatini	Elevates Soft Palate
Musculus uvulae	Shortens the uvula
Palatoglossus	Elevates and retracts the tongue
Palatopharyngeus	Elevates larynx
Salpingopharyngeus	Elevates larynx
Styloglossus	Retracts and elevates tongue
Stylohyoid	Elevates and retracts hyoid
Stylopharyngeus	Elevates larynx
Tensor veli palatini	Opens auditory tube; tenses soft palate

FIG. 2. The actions of the pharyngeal dilator muscles.

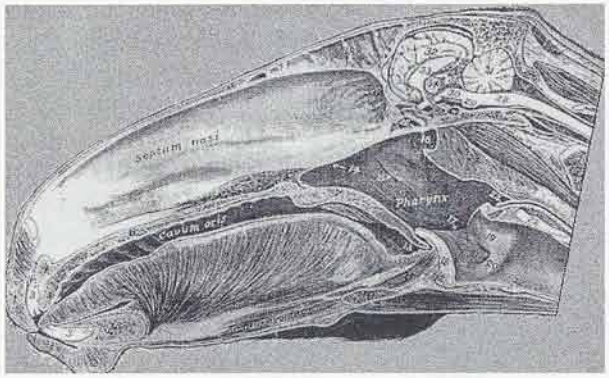

FIG. 3. Sagittal view of horse pharynx. During quiet respiration, the soft palate of the horse is in snug contact with the epiglottis because the larynx is locked into the nasopharynx. Air passes through the external nares, through the nasal cavities, through the larynx into the trachea. Simultaneously, liquid can be swallowed from the oral cavity, on either side of the larynx into the pharynx and esophagus. The tongue is located entirely within the oral cavity and is not situated in the pharynx.[3] (Reprinted from Getty (8), with the permission of W.B. Saunders.)

length of the adult tongue is shortest in the gibbon, longer in the chimpanzee, even longer in the orangutan and longest in the gorilla. The length of the oral cavity becomes smaller as one passes from an australopithecine the size of Mrs. Ples *to Homo erectus* to early and recent *Home sapiens*. But, because the posterior part of the tongue descended into the neck as the oral cavity became shorter, the tongue maintained its original length. (Fig. 6)

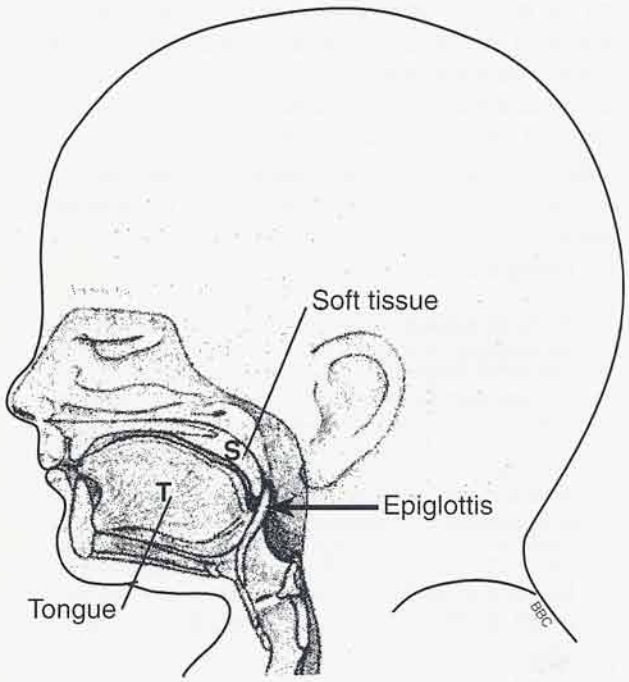

FIG. 4. Sagittal section of head of newborn full-term infant. The epiglottis is in direct contact with the soft palate (S) because the larynx is locked into the nasopharynx. In the newborn human infant the tongue is located entirely within the nasal cavity.[3] (Reprinted with the permission of Dr. Edmund Crelin.[9])

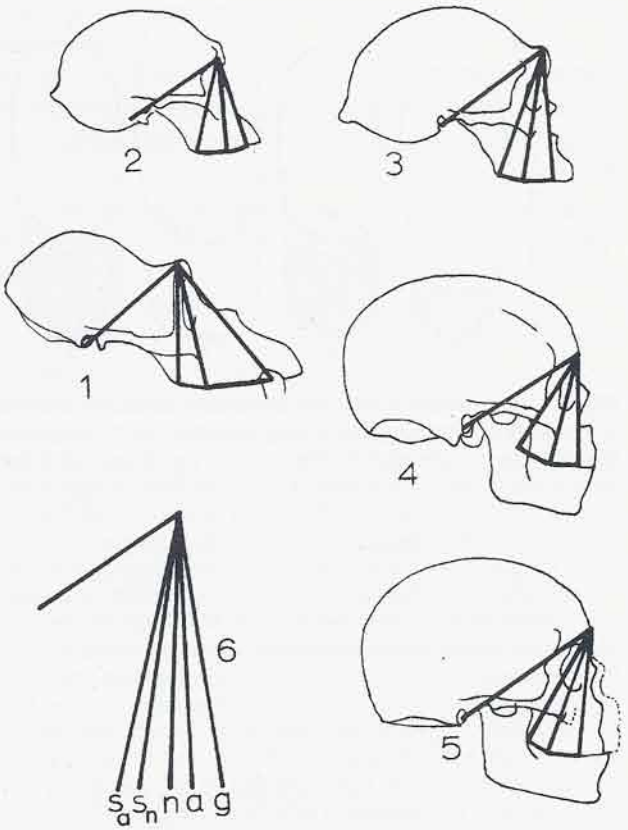

FIG. 5. Interpretations of the facial frameworks of a hominoid and a number of hominid species. A line drawn from the external auditory meatus to the apex of the supraorbital torus indicates how the facial framework is progressively "tucked" beneath the cranium in this series of animals. This kind of craniofacial flexion is described as "klinorynchy." **1,** Gorilla gorilla, a hominoid. The skull is markedly prognathous. **2,** Australopithecus africanus (Mrs. Ples', either ancestral to, or very close to the ancestry of, modern man. **3,** Homo sapiens neandertalensis (a primitive variety of man). **4,** Homo sapiens sapiens (modern man) **5,** Homo sapiens sapiens, an individual with extreme craniofacial flexion who represents phenotypic expression of an extreme variation in a parameter undergoing a phylogenetic change. **6,** The progressive development of craniofacial flexion in the above speciaes is demonstrated by the angle between the line joining the external auditory meatus and the supraorbital torus and the facial skeleton strut passing through the postorbital bar. **g,** Gorilla (67 degrees); **a,** Australopithecus (60 degrees); **n,** Homo sapiens neandertalensis (55 degrees) **Sn,** Homo sapiens sapiens (normal) (49 degrees); **Sa,** Homo sapiens sapiens (abnormal) (44 degrees). None of the values given are meant to be definitive; they are only indicative of the trend described.[9]

To accommodate to the smaller subcranial space, the tongue folds into the pharynx forming the anterior wall of the pharynx (Fig. 7). With the descent of the larynx and the development of a soft-walled oropharynx that supports speech, certain disadvantageous morphological characteristics also develop. The anatomical formation requires the pharynx to perform three distinct roles requiring totally different muscular activities: respiration, deglutition, and phonation. For deglutition, the

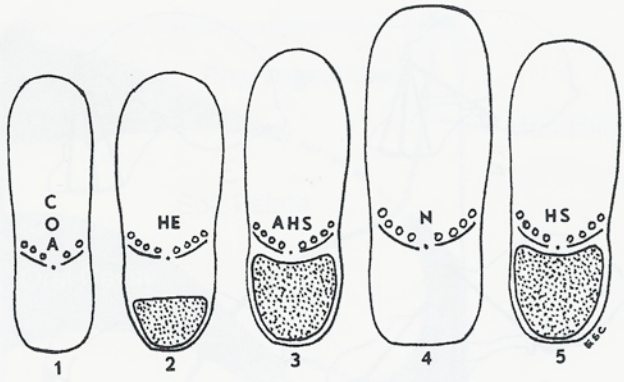

FIG. 6. "An illustration depicting the relative sizes and shapes of the adult homonid tongue during evolution. Each tongue is shown to be completely flat. The stippled areas represent the vertical part of the tongue when it forms the anterior wall of the oropharynx. The circles are the vallate papillae located along the junction of the anterior two thirds and the posterior one third of the tongue. The tongue labelled C, O, and A represents one from an adult male chimpanzee, an adult orangutan, or a man-ape australopithecine homonid, such as Mrs. Ples. The tongue labelled HE represents one of a *Homo erectus* homonid such as Peking woman. The tongue labelled AHS represents one of an archaic *Homo sapiens* homonid such as Steinheim woman. The tongue labelled N represents one of a classic Neanderthal homonid such as La Chapelle-aux-Saints. The tongue labelled HS represents one of a present-day *Homo sapiens* male. (Reprinted with the permission of Dr. Edmund Crelin.[3])

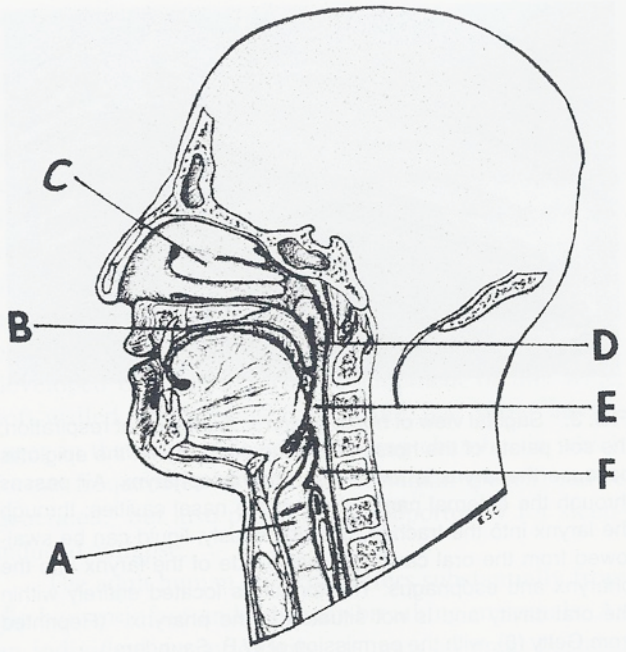

FIG. 7. Sagittal section of human adult pharynx. A: larynx, B: oral cavity, C: nasal cavity, D: nasopharynx (velopharynx), E: oropharynx, F: laryngopharynx (hypopharynx). The oropharynx extends from the tip of the uvula to the tip of the epiglottis. The oropharynx is unique to modern man. (Reprinted with the permission of Dr. Edmund Crelin.[3])

pharynx assumes the role of a flexible tube whose muscles, namely the pharyngeal constrictors, force food from the oral cavity into the esophagus. For phonation, the mature human pharynx is a muscular tube that can change in length and shape to alter the sounds passing through it. Once again, specific muscles alter the shape of the pharynx and larynx to perform this function. Finally, the pharynx must remain as a rigid tube to allow air passage without collapse during sleep. No muscle or group of muscles assumes this function as a primary role leaving the pharynx subject to collapse and obstruction during certain conditions of respiration. This allows for an occasional misdirected bolus of food to occlude the airway and for the pharyngeal airway to collapse under specific conditions of respiration.

In the presence of a patent nasal airway, using an evolutionary model to consider function of the soft palate and uvula, one could postulate that the soft palate and uvula, in the adult, continue to attempt to direct airflow toward the stable, nonflexible posterior pharyngeal wall. This mimics the airflow pattern achieved in situations where the uvula and epiglottis are interlocked. If this is true, then laser-assisted uvuloplasty (LAUP) and uvulopalatapharygoplasty (UPPP) may be detrimental to the patient's total recovery from OSA by removing the tissues that could potentially be utilized to direct airflow to the noncollapsible portion of the airway.

Because the oropharynx is unique to modern man and because modern man is the only mammal (with the possible exception of the brachycephalic English bulldog, an achondroplastic dwarf) to suffer from obstructive sleep apnea, it would seem reasonable to assume that the key to understanding the physiology and pathogenesis of obstructive sleep apnea may lie in the space between the uvula and epiglottis known as the oropharynx. This naturally assumes that all other factors (that is a normal size soft palate without excessive secondary folds, a normal size uvula, a patent nasal passageway, an oropharynx devoid of excessive tonsillar tissue or redundant tissue on the posterior pharyngeal wall) are equal.

Enlow and Hans[10] state

> The facial and pharyngeal airway is a space determined by the multitude of separate parts comprising its enclosing walls. The configuration and dimensions of the airway are thus a product of the composite growth and development of the many hard and soft tissues along its pathway from nares to glottis. Although determined by surrounding parts, those parts in turn are dependent upon the airway for maintenance of their own functional and anatomic positions. If there develops any regional childhood variations along the course of the airway that significantly alters its configuration or size, growth then proceeds along a different course, leading to a variation in overall facial assembly that may exceed the bounds of normal pattern. The airway functions, in a real sense, as a keystone for the face.

Attempts are being made to formulate a morphometric model[11] that uses intraoral measurements of the oral cavity in conjunction with body mass index (BMI) and neck circumference. Morphometric measurements of existing anatomical landmarks measure one or both of

two growth and development possibilities. Morphometric measurements measure the end result or outcome of growth and development either (1) by the way the skeleton influences the developing soft tissues or (2) by the way the developing airway determines the growth of the skeleton or by a combination of both.

Regardless of which element of the facial growths controls and determines the growth of the other, one comes to the conclusion that all anatomical measurements, whether they be morphometric, cephalometric or with CT or MRI, are actually measuring similarity or dissimilarity to animal, prehistoric man, and human infant. The data realized from these measurements could be interpreted as showing that the closer we are to a Neanderthal or animal-like structure, the less likely we are to have apnea.

The anterior pharyngeal wall, which is made up of the posterior border of the tongue, is paramount to the formation of OSA. The next logical assumption has to be that the primary pathogenic anatomical cause of OSA is the posterior border of the tongue. Roberts[6] states that as the mandible is moved forward, the soft palate and uvula follow. Therefore, removal of the uvula and soft palate would seem to be unnecessary for the resolution of OSA, once again granting that the neither the nasal passages nor velopharynx or oropharynx is obstructed with redundant tissue. In fact, excision of the uvula and soft palate may actually increase the likelihood of OSA if the soft palate's function is to direct airflow toward the posterior wall of the pharynx. It would be logical to assume that if the tongue could be moved out of the oropharynx immediately prior to the apneic incident, then the obstructive incident would not occur (once again granting that neither the nasal passages nor velopharynx or oropharynx is obstructed with redundant tissue). Indeed research shows a high degree of treating OSA with a tongue-retaining device.[12,13]

CONCLUSION

This paper traces the development of the adult human pharynx from air-breathing vertebrates other than man, through the evolutionary development of modern man and through maturation from infancy to adulthood. It presents the hypothesis that because the adult human pharynx developed an oropharynx, not present in other air-breathing vertebrates, as a result of the evolvement of upright posture and speech; the adult human did not ontogenetically develop specific musculature to dilate and maintain dilation of the pharynx. A corollary to this hypothesis might state that if an interlocking soft palate and epiglottis were evolutionarily responsible for maintaining a patent airway in obligate nose-breathing mammals, these organs might still be responsible, in the mature human, for the direction of laminar airflow. It would, therefore, stand to reason that surgical excision of the uvula and soft palate might eventually lead to a more critical problem in the patient's long-term follow-up. It would also be reasonable to assume that treatment of OSA should be centered upon maintaining patency in the oropharyngeal region of the pharynx, with particular attention paid to the anterior wall of the oropharynx, that is, the posterior border of the tongue.

If the development of the airway is indeed crucial to the development of the facial structure and if development of skeletal structure is a critical factor in the occurrence of OSA as a child ages, it is essential to be able to forecast which children will develop OSA. Interceptive treatment could then be instituted in one of two ways:

(a) Continuous positive air pressure (CPAP) applied early in the development of the adult pharynx to controls size of the upper airway and thus guide development of the skeletal structure, or
(b) Early orthodontic interception to guide development of the skeletal structures.

Phylogeny and otogeny should be considered when developing treatment modalities for OSA.

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Medical hypothesis

The Great Leap Forward: the anatomic basis for the acquisition of speech and obstructive sleep apnea

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Abstract

Obstructive sleep apnea is an anatomic illness caused by evolutionary changes in the human upper respiratory tract. These changes include shortening of the maxillary, ethmoid, palatal and mandibular bones, acute oral cavity-skull base angulation, pharyngeal collapse with anterior migration of the foramen magnum, posterior migration of the tongue into the pharynx, descent of the larynx and shortening of the soft palate with loss of the epiglottic–soft palate lock-up. While it is commonly believed that some of these changes had positive selection pressures for bipedalism, binocular vision and locomotion, development of voice, speech and language ultimately became a substantial contributing factor. Here it is shown that these changes are the anatomic basis of obstructive sleep apnea.

Keywords: Obstructive sleep apnea; Sleep disordered breathing; Upper respiratory tract; Anatomy; Evolution

1. Introduction

With the possible exception of brachycephalic dogs, such as the English Bulldog, man is the only mammal that experiences obstructive sleep apnea (OSA) [1,2]. The adult *Homo sapiens* supralaryngeal vocal tract (SVT) differs from that of close ancestors and other mammals by: the presence of a short face or splanchnocranium made up of the mandible, palate, ethmoid, maxilla and sphenoid; a narrow elongated supralaryngeal vocal tract (SVT); an anterior foramen magnum and oropharyngeal tongue; a descended larynx and shortened soft palate with loss of the epiglottic–soft palate lock-up; and an acute oral cavity–skull base angle (Table 1). These anatomic features facilitated man's ability to speak and to develop language (Table 2). This very same anatomy, a product of man's evolution, predisposed man to the development of OSA.

The natural selection pressure for speech and language was so strong that the undesired consequence of OSA was carried forward to modern man. Based on this reasoning, obstructive sleep apnea is an anatomic illness.

As the terminology for this region can be confusing, Table 3 defines the overlapping nomenclature.

2. Acquisition of speech

Speech and the ability to communicate separated man from the remainder of the animal kingdom and permitted humans to evolve into advanced civilization. Jared Diamond, a physiologist at UCLA, has labeled this evolutionary change 'The Great Leap Forward' [3]. Diamond postulates that The Great Leap Forward occurred approximately 40 000 years ago (40 ka). Prior to that, man possessed tools and a sizeable brain, but little progress had occurred for hundreds of thousands of years. Forty ka ago, the SVT anatomy and the necessary neural connections were completed so that man could speak and create language. Diamond sites strong selection pressure for voice, speech and language. This pressure was a substantial contributing factor for evolutionary change in the anatomy of the SVT [3].

One can easily imagine the survival advantage of those groups that could speak over those that could only grunt. Speaking humans could communicate messages pertaining to defense and food acquisition and could learn from the generations that came before them. Prior to the presence of

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Table 1
Anatomic changes facilitating speech[a]

Short maxilla/mandible
Short ethmoid and palate
Anterior foramen magnum
Acute cranial base angulation
Oropharyngeal tongue
Descended larynx
Shortened soft palate
Loss of epiglottic–soft palate lock-up
Narrow, distensible supralaryngeal vocal tract (SVT)
1:1 ratio of the SVT_V to SVT_H

[a] The SVT includes the larynx, pharynx, nasal cavity and oral cavity. SVT_V is the vertical segment and SVT_H is the horizontal segment.

speech, information was acquired slowly and knowledge was not easily passed on. With speech came language and then the written word. When language was developed and then recorded, massive bodies of knowledge were accumulated. Man could now learn from more that his own experiences. The following excerpts summarize Diamond's reasoning [3].

> The identity of the ingredient that produced the Great Leap Forward poses an archaeological puzzle without an accepted answer. It doesn't show up in fossil skeletons. It may have been a change in only 0.1 percent of our DNA. What tiny change in genes could have had such enormous consequence?Like some other scientists who have speculated about this question, I can think of only one plausible answer: the anatomical basis for spoken complex language.The answer seems to involve the structure of the larynx, tongue, and associated muscles that give us fine control over spoken sounds. Like a Swiss watch, all of whose many parts have to be well designed for the watch to keep time at all, our vocal tract depends on the precise function of many structures and muscles.That's why it's plausible that the missing ingredients may have been some modifications of the protohuman vocal tract to give us finer control and permit formation of a much greater variety of sounds.It's easy to appreciate how a tiny change in anatomy resulting in capacity for speech would produce a huge change in behavior. With language, it takes only a few seconds to communicate the message, "Turn sharp right at the fourth tree and drive the male antelope toward the reddish boulder, where I'll hide to spear it." Without language, two protohumans could not brainstorm together about how to devise a better tool or about what a cave painting might mean. Without language, even one protohuman would have had difficulty thinking out for himself or herself how to devise a better tool.

Table 2
Anatomic requirements and SVT changes for modern speech

Requirements	Changes
1:1 ratio SVT_V to SVT_H	Klinorynchy
	Laryngeal descent
Buccal speech	Laryngeal descent
	Shortened soft palate
	Loss of epiglottic–soft palate lock-up
Narrow, distensible, angulated SVT	Klinorynchy
	Anterior migration of foramen magnum
	Oropharyngeal tongue
	Acute craniobase angulation

3. Hypothesis

The anatomic piece of the Great Leap Forward is a 1:1 ratio of the vertical (SVT_V) to horizontal (SVT_H) portions of the SVT. SVT_H includes the vocal tube from the lips to the pharynx. SVT_V includes the vocal tube from the pharynx to the vocal cords [4], Additional required changes include buccal speech and a narrow, distensible, angulated SVT. The hypothesis is that the anatomic changes that created this SVT contributed to *Homo sapiens*' recent upper respiratory tract evolution and resulted in the development of obstructive sleep apnea (OSA).

4. Methods

Comparative anatomy and the principle of ontogeny recapitulates phylogeny were used to examine the evolutionary changes from pre-hominid primates to anatomically modern (a.m.) *Homo sapiens*. *Pan troglodytes* is a.m. *Homo sapiens*' closest living primate relative [3], and is used for much of this comparison.

5. Klinorynchy

Laurence Barsh describes klinorynchy as the posterior migration of the splanchnocranium (facial skeleton) under the neurocranium (brain case) [1]. This has resulted in several changes in the maxilla, palate, ethmoid and mandible. According to study of the phylogenetic evolution of the splanchnocranium, the maxilla and other facial bones moved posteriorly [5,6]. The mandible followed, moved posteriorly, and rotated downward, as reflected in an obtuse gonial angle. Absent other change, this posterior migration would cause the pharynx to be compressed. In order to preserve the pharynx for both respiration and deglutition, the mandible, maxilla, ethmoid and palate were shortened. Fig. 1 morphs the common chimpanzee to modern man, showing these changes.

Further evidence of this change is seen in the teeth. The dentition in man is crowded, as proven by the fact that man is the only primate with impacted third molars. David Roberts writes, "It is well known that dentitions are more

Table 3
Terms[a]

Upper respiratory tract	The air passage above the vocal cords, including nose, nasopharynx, oropharynx and larynx
Upper aerodigestive tract	Upper respiratory tract plus the hypopharynx and oral cavity. Includes the nose, oral cavity, nasopharynx, oropharynx, hypopharynx, and larynx. If one opens the mouth, the oral cavity becomes part of the upper respiratory tract. With this inclusion, the only difference between the upper respiratory tract and the upper aerodigestive tract is the hypopharynx
Supralaryngeal vocal cord tract (SVT)	The voice passage from vocal cords to oral lips; therefore the supraglottis, oropharynx and oral cavity. The vertical segment, SVT_V, extends from the vocal cords to the top of the oropharynx. The horizontal segment, SVT_H, extends from the lips to the posterior wall of the pharynx
Obstructive sleep apnea (OSA)	Disruption in sleep caused by anatomic obstruction in the upper respiratory tract.
Sleep disordered breathing (SDB)	A broader category of breathing disorders during sleep, including OSA, snoring, Cheyne Stokes breathing, hypoventilation syndrome, upper airway resistance syndrome (UARS). SDB and OSA are often used interchangeably. SDB is increasingly the preferred term among sleep medicine experts
Klinorynchy	The migration of the splanchnocranium (face) under the neurocranium [1,5]
Homo sapiens	Genus and species of man, anatomically characterized by "a high round cranium, a chin, a small orthognathic face, as well as reduced masticatory apparatus and brow ridges." [13]. Anatomically modern *Homo sapiens* first appeared 250–300 ka and is designated as a.m. *Homo sapiens* or as subspecies *Homo sapiens sensu stricto*

[a] As different definitions describing the upper respiratory tract have been developed for different purposes, the nomenclature is overlapping and potentially confusing. These are terms used in this paper.

conservative in terms of genetic change than are other parts of the skeleton" [5]. A.E.W. Miles writes, "In summary, over the past 20 million years or so man's dentition has been slower to change than other parts of him" [7]. This is shown schematically in Fig. 2.

A noteworthy part of this change is that as the dental arches shorten, they expand laterally. This has obvious implication for expansive orthodonture to prevent OSA. These effects, namely foreshortening of the maxilla, palate, ethmoid and mandible, resulted in the shortening of the oral cavity (SVT_H) and contributed to the narrowing of the pharynx [4].

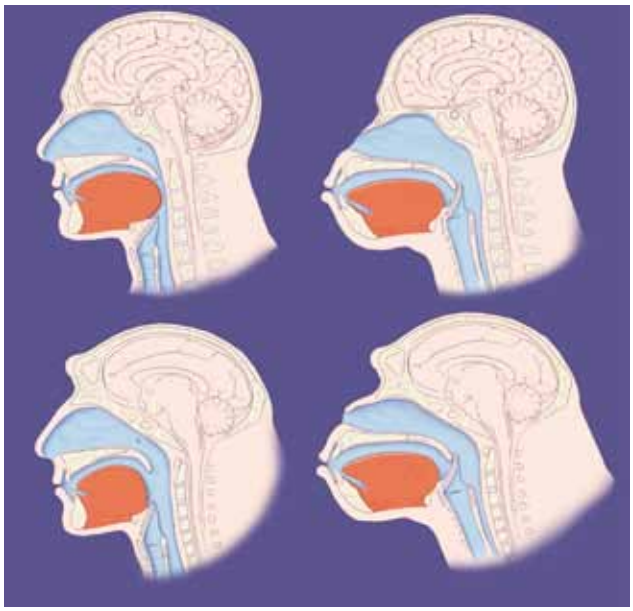

Fig. 1. Klinorynchy as demonstrated by the evolution from *Pan troglodytes* to *Homo sapiens*. The lower right figure is a midsagittal view of *Pan troglodytes*. The upper left figure is a midsagittal view of *Homo sapiens*, with the tongue drawn in the awake position, i.e. with the tongue base pulled forward. The upper right figure shows the splanchnocranium of *Pan troglodytes* combined with the neurocranium of *Homo sapiens*. The lower left figure shows the neurocranium of *Pan troglodytes* combined with the splanchnocranium of *Homo sapiens*. The key changes have not been driven by the expansion of the neurocranium over the mid-face, but rather the retrusion and inferior rotation of modern man's mid and lower face. Visible Productions, 2001.

6. Laryngeal descent

V.E. Negus describes descent of the larynx in the classic text, *The Comparative Anatomy and Physiology of the Larynx*. Negus reviews comparative anatomy of the larynx beginning with the earliest creature that ventured from water onto land for food or burrowed in the mud and was forced to breathe air during the dry season. He then follows the progression of the organ. The larynx evolved very early as a protective sphincter for the air-containing sac that ultimately became the lungs. Negus views the larynx as an organ developed primarily to separate the alimentary and respiratory tracts [8].

Negus describes the evolution of the larynx in relation to the development of speech, "From the observation of all species in respect to their anatomical structure and their physiological necessities, it is concluded that the primary function of the epiglottis is to subserve the sense of smell" [8]. As many animals are dependent on their sense of smell to detect prey and to avoid noxious foods and dangerous predators, it was mandatory for the olfactory tract to be open at all times, especially during inspiration, expiration and deglutition.

The larynx and the epiglottis in all animals reside superior to the oropharynx. In many mammals, including dolphins, bears and dogs, the larynx sits at the skull base. The monkey's larynx is between the skull base and the first cervical vertebrae. The cat and the squirrel have the lowest

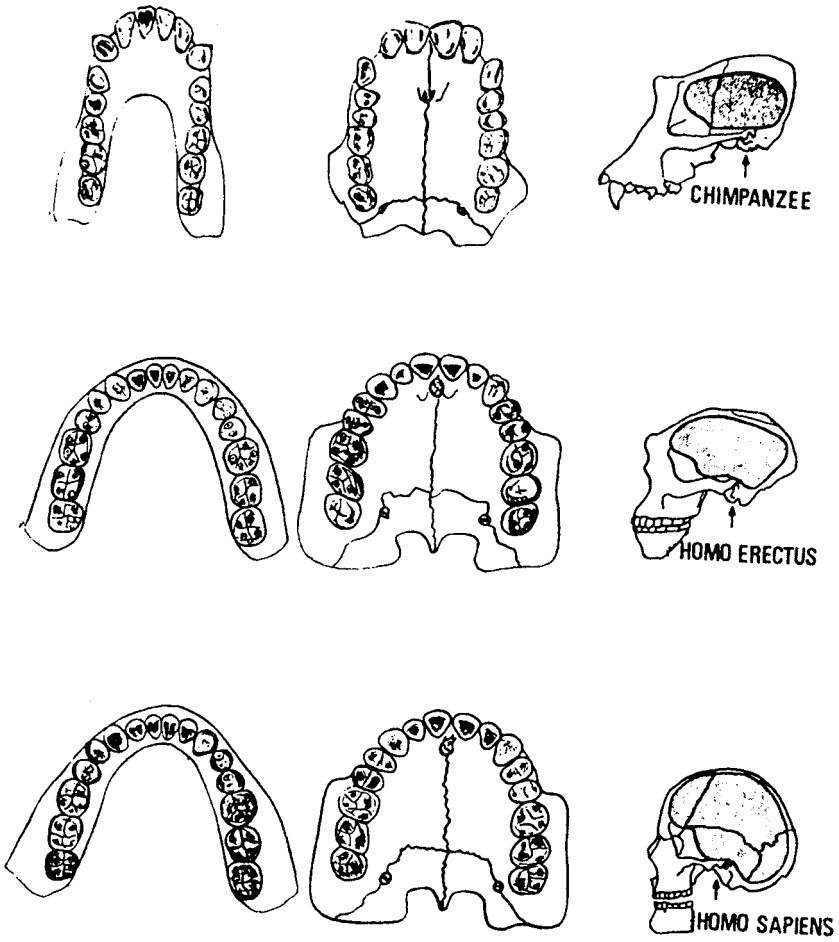

Fig. 2. Maxillae of *Pan troglodytes*, *Homo erectus* and *Homo sapiens*. *Homo sapiens*' maxilla is short and wide. The teeth are crowded. The shortening of the maxilla is depicted in the lateral views. The arrows on the figure's right depict the anterior rim of the foramen magnum and serve as a reference point for the posterior pharynx. Note the narrowing of the pharynx as depicted by the distance from the posterior maxilla to the anterior foramen magnum. From Miles [7]. Reprinted by permission from The Royal Society of Medicine.

lying larynx, which resides at the top of the first cervical vertebrae.

Only man has a descended larynx. The larynx is located between the third and fourth cervical vertebrae in the human newborn and is located at the bottom of the fourth cervical vertebrae in the human adult, as depicted in Fig. 3. Fig. 4 shows these relationships in the dog, the chimpanzee, the infant human and the adult human. In terms of the relationship between soft palate and epiglottis, it is found that the majority of animals do not have a uvula. Instead, the soft palate extends posteriorly and inferiorly, further separating the airway from the alimentary tract. The uvula, in fact, is the remnant of the long soft palate [8].

Negus' view of the evolution of speech is summarized as follows. As primates assumed an upright position, they began to rely more on vision than olfaction. This permitted the degeneration of the sense of smell and liberated the soft palate [8].

The degeneracy of the sense of smell liberated the soft palate from the necessity of contact with the epiglottis and allowed a gap to be interposed between the two. After separation had occurred it became easy for laryngeal sounds to escape from the mouth and for the oral cavity and lips to enter into the formation of vowel sounds and consonants.

The lock-up between the soft palate and epiglottis is seen throughout the animal kingdom. Fig. 5 shows the epiglottic–soft palate lock-up in the goat, C*apra hircus*. It is only in man that this lock-up is lost, due to laryngeal descent and shortening of the soft palate. These changes allowed man to acquire buccal speech.

7. Oropharyngeal tongue

Crelin notes that man is the only animal whose tongue resides partially in the pharynx. In all other animals, including non-human primates, the tongue resides exclusively in the oral cavity. Crelin does not clarify whether the

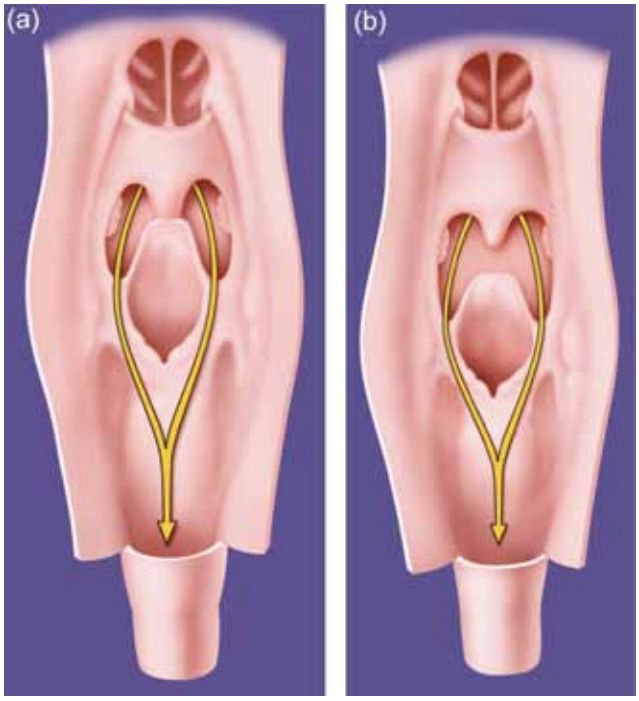

Fig. 3. Epiglottic–soft palate lock-up as viewed from the posterior pharynx. (a) In the human infant, the epiglottis overlaps the soft palate and food is diverted laterally around the epiglottis. Alimentation and respiration can occur concurrently. In animals, there is no uvula and the soft palate hangs like a curtain, further separating the alimentary and respiratory tracts. (b) In the human adult, the larynx is descended, the soft palate is shortened and the epiglottic–soft palate lock-up is lost. While food theoretically channels around the larynx, there is constant risk of aspiration. As Charles Darwin wrote, "…every particle of food and drink which we swallow has to pass over the orifice of the trachea, with some risk of falling into the lungs, notwithstanding the beautiful contrivance by which the glottis is closed" [12]. Visible Productions, 2001.

human oropharyngeal tongue is a result of the shortened oral cavity, descent of the larynx or some other reason [9].

Negus also describes the retro positioning of the tongue. Negus opines that the tongue is primarily designed for mastication and that a shorter tongue would do for bolus formation. As klinorynchy progressed and the jaws receded, the tongue was pushed posteriorly. The human oral cavity is far smaller than that of a similar sized non-hominid primate, yet the tongue remains approximately the same volume. The tongue is therefore oversized, and according to Negus, has thus pushed the larynx inferiorly. The tongue now protrudes into the oropharynx and whereas in most animals the tongue is relatively flat, the tongue in man is curvilinear, bulky, and folds both posteriorly and inferiorly [8].

It seems more likely that the larynx descended to enable speech. The tongue followed the laryngeal descent and filled the pharynx. The undulating dorsal lingua of an open mouthed gospel singer is a persuasive example of the tongue's role in speech. Perhaps it is not by accident that humans have an oropharyngeal tongue, but rather by design, for this organ facilitates both speech and deglutition.

8. Pharyngeal collapse and anterior migration of the foramen magnum

Crelin also examines the base view of the skull. He notes that in adult a.m. *Homo sapiens* the space from the palate to the foramen magnum is shorter than the same space belonging to other adult primates. In addition, Crelin writes that the base of the newborn and young *Homo sapiens* skull was similar in proportion to the adult chimpanzee and other non-hominid primates. The distance and space between the posterior palate and anterior foramen magnum indicates that this space was available for the pharynx. For purposes of olfaction, bigger is better. For purposes of speech, smaller is better and this is exactly what evolved in humans. Examination of primate skulls shows that the foramen magnum is located more anteriorly, the closer one gets to modern man [9]. While it is opined that this is a favorable change for man's upright stance, it can also be argued that man requires a narrow, distensible pharynx to facilitate speech.

The anterior migration of the foramen magnum is also part of the evolutionary change to facilitate speech. This is seen in Fig. 2.

9. Craniobase angulation

Craniobase angulation is the relationship between the maxilla, ethmoid, sphenoid and basioccipital bones. This is the bend in the two-tube SVT, the angulation between SVT_V and SVT_H. Lieberman and McCarthy examine the ontogeny of cranial base angulation in humans and chimpanzees. They report that craniobase angulation occurred early in *Homo sapiens*, and that flexion is seen in humans whereas extension is found in non-human primates. In a.m. *Homo sapiens*, the cranial base flexes 8–16° postnatally, but in *Pan troglodytes* (common chimpanzee) 15–28° extensions are seen. Accepting the premise that ontogeny recapitulates phylogeny, these changes contribute to the rotation aspects of klinorynchy. Lieberman postulates that this created an advantage for the development of speech, for the acute angle between SVT_V and SVT_H facilitates speech [10].

10. Speech

Lieberman describes human language from an evolutionary perspective in his book *Eve Spoke*. The production of speech begins in the larynx. As the vocal cords adduct and air is expelled, a sound is produced. This is called the pitch [11].

> The major factor that differentiates words in all human languages, however, is not the pitch of a person's voice. The tube above the larynx, called the supralaryngeal vocal tract (SVT) like the clarinet's tube, filters the sound

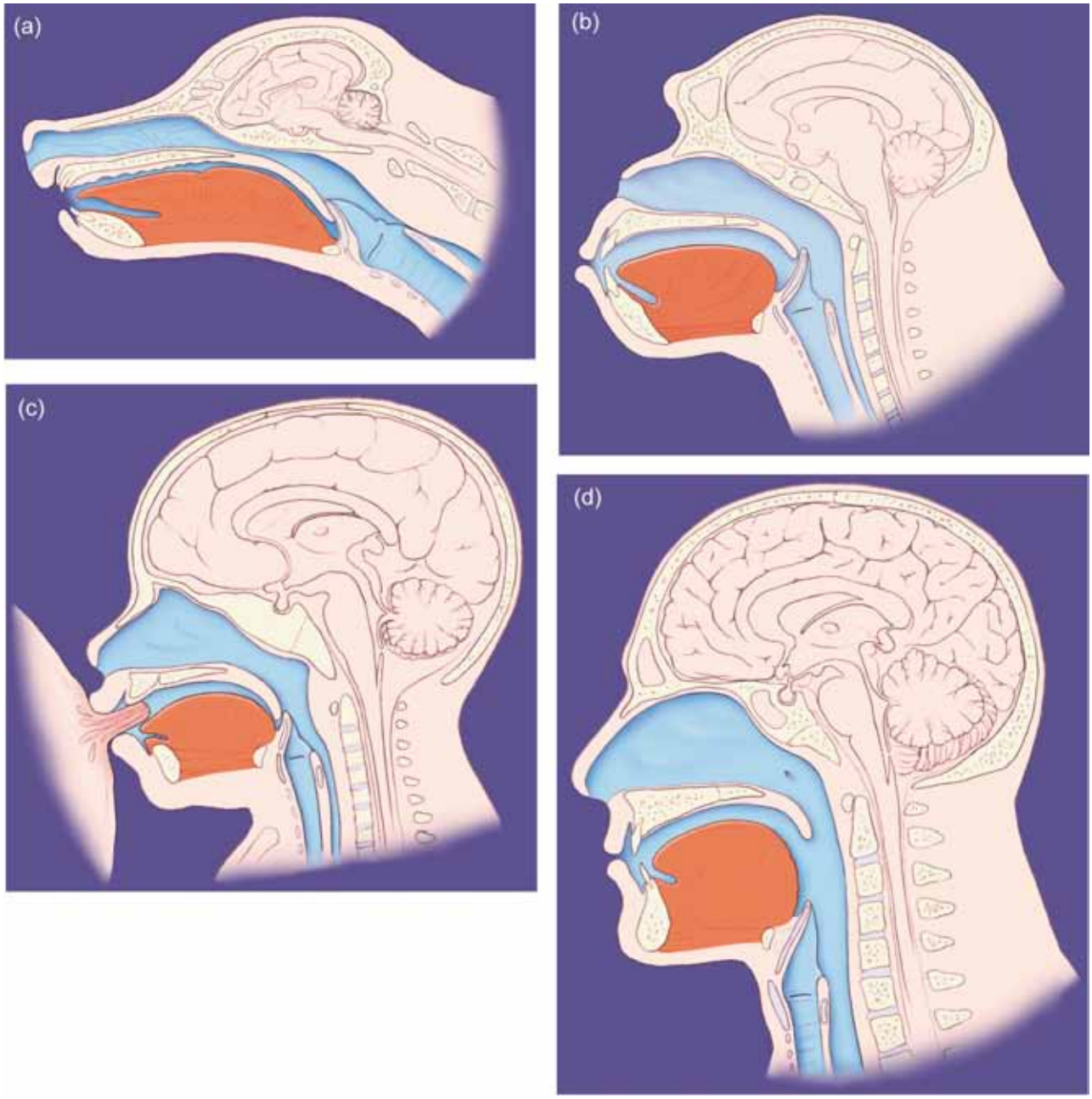

Fig. 4. The epiglottic–soft palate relationship and the descent of the larynx. (a) In the dog, *Canis familiaris*, the tongue resides exclusively in the oral cavity, the epiglottis and soft palate are locked up and the larynx resides high in the neck. (b) In the common chimpanzee, *Pan troglodytes*, the tongue resides exclusively in the oral cavity, the epiglottic–soft palate relationship persists and the larynx is high. (c) In the infant *Homo sapiens*, the epiglottic–soft palate lock-up persists (ontogeny recapitulates phylogeny), the larynx is high and the tongue is primarily in the oral cavity. As the juvenile matures, the larynx descends and the tongue falls into the pharynx. (d) In the adult *Homo sapiens*, the epiglottic–soft palate lock-up is lost. The larynx is descended. The tongue protrudes into the pharynx. Visible Productions, 2001.

> produced by the larynx.Changing the position of the pharynx, tongue and lips produces speech. The nasal cavity plays a minor role in speech production.

The structure of the SVT provides man with the ability to vocalize the vowels and consonants that constitute human speech. Lieberman and others point out that the major disadvantage of the SVT is that food can be accidentally inhaled. He points out that in 1859 Darwin noted, "…the strange fact that every particle of food and drink we swallow has to pass over the orifice of the trachea with some risk of falling into the lungs" [11,12]. Lieberman writes [11],

> The human vocal tract has other liabilities. Our mouths and jaws are shorter than those of non-human primates are. If you compare a human jawbone and upper jaw with a Neanderthal's it becomes obvious that there is lots of space for Neanderthal

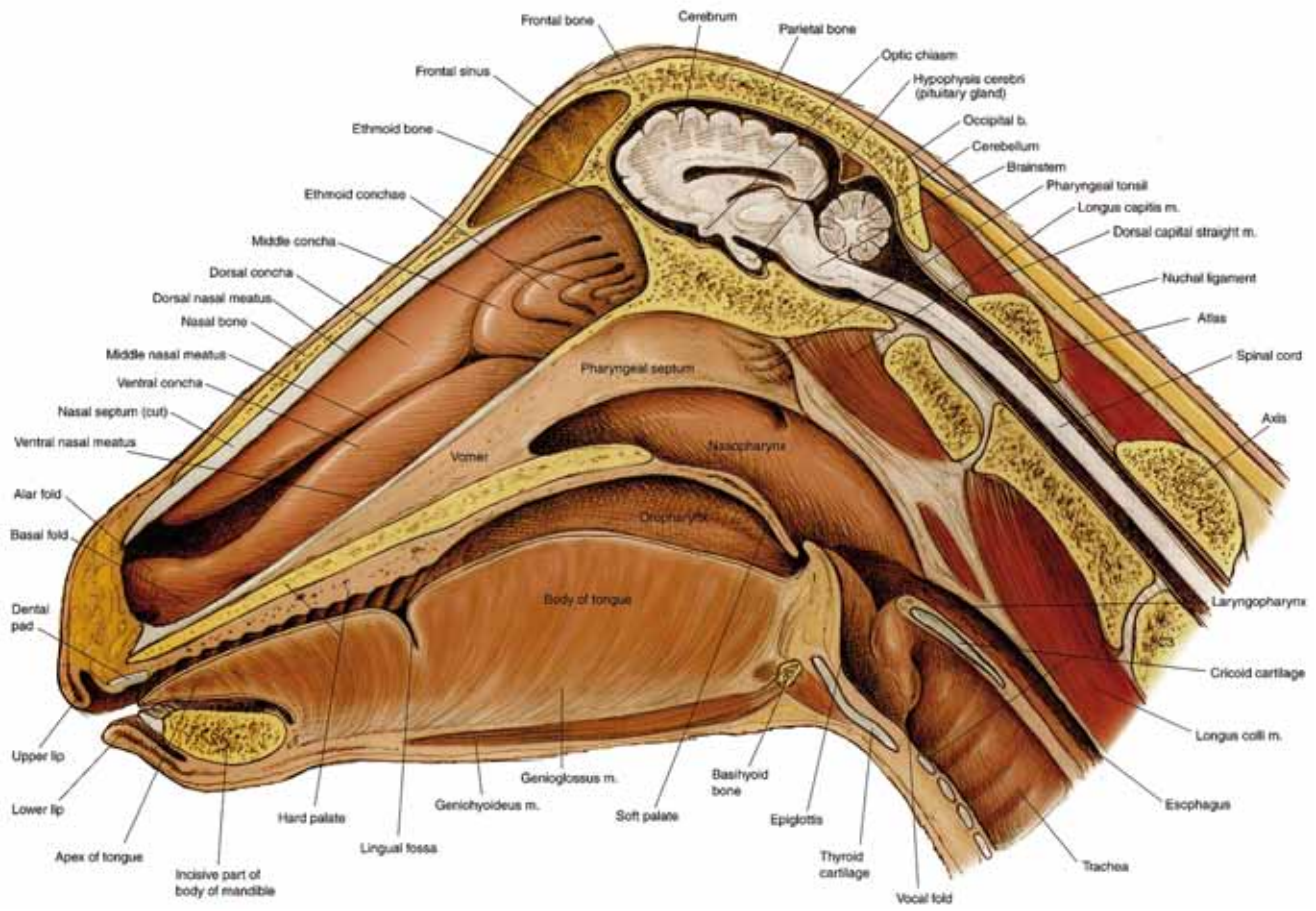

Fig. 5. Midsagittal view of *Capra hircus* (goat). Note the high position of the larynx relative to the descended position in man, the relationship of epiglottis to soft palate (epiglottic–soft palate lockup), the facial projection, the long maxilla and mandible, the length of the sphenoid bone, the obtuse craniobase angle, the long palate to foramen magnum distance, and the small, flat tongue, which resides exclusively in the oral cavity. From McCracken TO, Kainer RA, Spurgeon TL. Spurgeon's color atlas of large animal anatomy. Philadelphia: Lippincott Williams & Wilkins, 1999; p. 83. Reprinted by permission from Lippincott Williams & Wilkins, ©1999.

teeth. Neanderthals never had impacted wisdom teeth. Though our teeth are smaller than those of Homo erectus or Neanderthals, there is less room for them.

Negus also recognizes the problems of the modern SVT. According to Lieberman, Negus makes it clear that, [8,11]

> The right angle bend in the human vocal tract also reduces the respiratory efficiency of our upper airways. So we can conclude that having a human vocal tract with a low larynx increases our chances for immediate death by asphyxiation, increases the chances for a slower death by infection from impacted wisdom teeth, reduces the chances of survival when food supplies are limited (the 'normal' condition for most people past and present) and restricts breathing to a degree. In fact, the *only* function that is better served is speech production.

There is a cognitive piece to this story. Simply having a modern SVT is not the only necessary component for speech and language. Though the neural connections and development are not described here, the brain clearly had to evolve as well.

11. 1:1 Ratio of the SVT

A great deal of attention has been directed toward modeling the SVT. This allows the linguist to study speech production. Vowel formation is the most important element of speech, and it is generally accepted, primarily from computer models, that the maximum vocal clarity occurs when the length of the oral cavity (SVT_H) and the length of the pharynx ($SVT_{V)}$ are approximately equal, i.e. the ratio of oral cavity to pharyngeal length is approximately 1:1 [4,11]. This is shown in Fig. 6. Lieberman argues that Neanderthals would not have been able to articulate as well as modern man, because, given the length of the Neanderthal's oral cavity, the larynx would have been descended into the chest. *Homo sapiens* is not a descendant of *Homo neanderthalis*. Lieberman presumably uses this example to show the importance of klinorynchy with laryngeal descent.

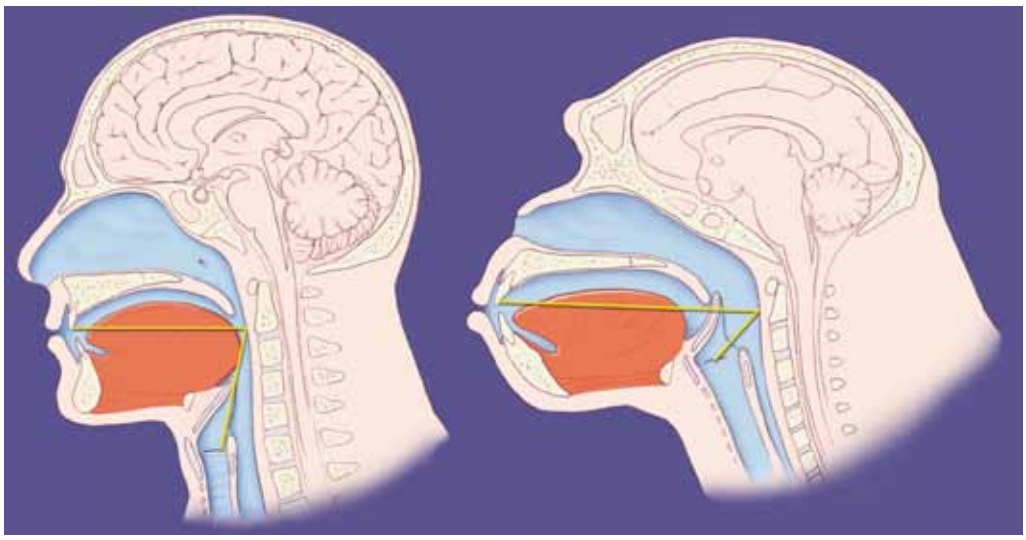

Fig. 6. Ratios of distances from incisor to pharynx and pharynx to larynx in *Homo sapiens* and *Pan troglodytes*. The 1:1 SVT_V to SVT_H ratio is shown on the left. For comparison, the same ratio for the common chimpanzee is shown on the right. Visible Productions, 2001.

Neanderthals have been used as the generic robust stone age man. This is depicted in a drawing from Lieberman's text, and reproduced in Fig. 7. This is an important point, because the evolution of the SVT to optimize speech required an oral cavity and a pharynx equal in length. The descent of the larynx and the shortening of the oral cavity accomplished this.

The angulation between the pharynx and oral cavity enhances the ability to produce vowel sounds [9]. While one could argue that this angulation was part of man's adoption of an upright posture, it may have evolved to enhance speech [10].

12. Evolution vs. revolution

Was there an adverse selection for sleep apnea? Other than an occasional snorer who was killed by his cavemates, most likely there was not negative selection for sleep apnea. The adverse health consequences of OSA do not manifest until the age of 40–60 years, an age well past most reproductive activity and until recently, past the life expectancy of *Homo sapiens*.

The issue of when these anatomic and behavioral changes occurred is still an issue of great discussion among modern anthropologists [13]. There is controversy over whether the changes occurred rapidly, i.e. a revolution in 40–50 ka, or more slowly, first appearing 250–300 ka ago. The vast body of literature on this subject has other explanation for the anatomic changes discussed herein. Most focus on bipedalism, binocular vision and locomotion.

This paper does not side with any one theory. The described changes may have had selective advantage for reasons other than speech. The important point is that speech contributed to upper respiratory tract evolution and the changes that occurred in the SVT anatomy. These changes, perhaps the final changes in the upper respiratory tract, had the adverse outcome of obstructive sleep apnea.

13. Discussion

To recapitulate, modern *Homo sapiens*' upper respiratory tract anatomy evolved for several reasons. One reason was to facilitate speech. The pharynx was narrowed to form a narrow, distensible tube for better sound modulation by rotation of the foramen magnum anteriorly, migration of the palate posteriorly and shifting of the tongue into the oropharynx. Oral/buccal speech was generated as the larynx descended and the soft palate shortened, causing loss of the epiglottic–soft palate lock-up. A 1:1 ratio of the SVT_V to SVT_H, vocal cords to pharynx and pharynx to incisors/lips was created by laryngeal descent and klinorynchy, the foreshortening of the face by contraction of the ethmoid, maxilla, palate and mandible. Craniobase angulation further improved vocal quality.

The obstructing anatomy is clearly a soft tissue phenomenon, as it is absent during the day and is present at night. The soft tissue is suspended and supported by the underlying skeleton. Soft tissue obstruction sites during sleep include the nose, upper and lower pharynx and occasionally the larynx. The premise of this paper is that the changes in skeletal anatomy have positioned the soft tissues so that they now obstruct respiration during sleep. Obesity and old age compound sleep disordered breathing (SDB), obstructive sleep apnea (OSA) included.

SDB is a prevalent, morbid and mortal illness [14,15] affecting 24% of adult males and 9% of adult females [16]. SDB is a risk factor for hypertension [12–19]. It causes early death by stroke and heart attack. It complicates all cardiovascular disease, especially for those with angina, heart failure, TIAs, and for CVA survivors. SDB

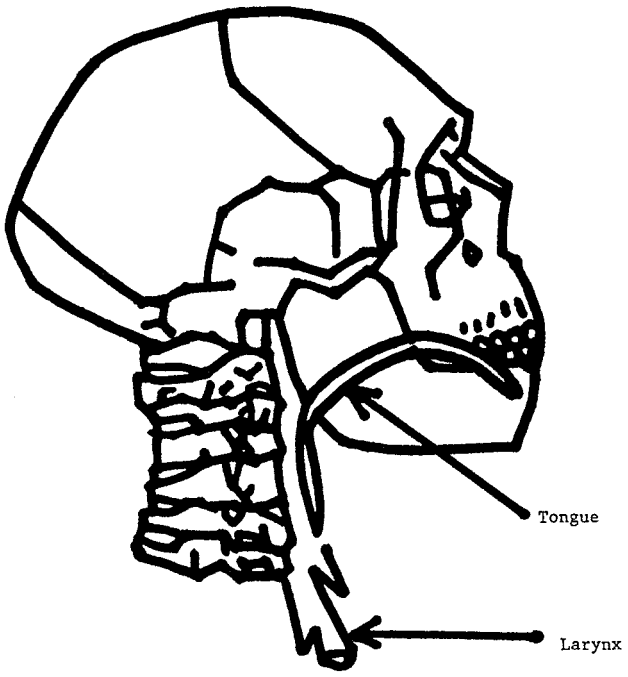

Fig. 7. Why a Neanderthal could not have a human vocal tract. "If we place a modern human tongue that corresponds to a mouth and pharynx that have equal lengths on the 'classic' La Chapelle-aux-Saints fossil, the larynx ends up positioned *below* the neck. That's most unlikely. The tongue contour for this sketch was derived from cineradiographic studies of living humans talking by Peter Ladefoged and his colleagues at UCLA; it is the tongue of a normal adult woman. A smaller tongue would not be able to push food backward and downward to allow the Neanderthal to swallow. The spinal column of the Neanderthal is modern and has the lordosis, or curvature, of a normal human adult. The skull is also positioned on the standard 'Frankfurt' plane used to compare the skulls of various primates. The problem arises because the length of the Neanderthal mouth is outside the range of modern human beings. William Howells at Harvard University established this fact by studying different human population groups." From Lieberman [11], p. 93. Reprinted by permission from W.W. Norton & Co. Inc, ©1998.

predisposes to accidents on the road, at home and at work. SDB causes daytime sleepiness with loss of creative productivity, diminished personal energy and failing personal relationships, since snoring is associated with bedroom disharmony. SDB is also associated with heart failure, hypercapneic COPD, nocturia, retinal hemorrhage, epilepsy and pacemaker dependant arrhythmia [14,15].

14. Conclusion

OSA is an adverse consequence of man's upper respiratory tract evolution. Speech was a substantial contributing factor. This has important implications for further study. Anthropologists must add this to their study of evolutionary change. Investigation of the genetics of craniofacial growth and development as well as the genetics of growth and development of the SVT is essential to current and future knowledge. Perhaps we can genetically modify or orthodontically create a larger or wider mandible and maxilla. Given that we do not want to impair speech, is it possible to genetically or surgically modify the mandible, maxilla, palate, pharynx and tongue to maintain vocal quality, to reduce the propensity for OSA? It may be that the oropharyngeal tongue must be studied by neurobiologists with the goal of making this a muscle of respiration, which contracts during sleep [20]. Perhaps there are other contributing soft tissue changes such as a floppy epiglottis or lax pharyngeal musculature.

Most of the anthropologic study has focused on the lateral view, i.e. the sagittal section, and to a lesser degree, on the base view (axial examination). Study is needed for the axial and coronal perspectives.

Is the SVT still evolving? Can the situation worsen? Are we raising a society condemned to nightly positive airway pressure (CPAP) for the second half of their lives? It should be obvious that these evolutionary changes are also the anatomic basis for difficult laryngoscopy and intubation. The descended larynx, the oropharyngeal tongue and the acute craniobase angulation are the primary contributors. Mandibular and maxillary shortening are contributing factors for infection and dysfunction associated with unerupted third molars. This may contribute to temporomandibular joint dysfunction syndrome and orthodontic issues as well. Foreshortening of the maxillary and ethmoid bones may have squeezed the osteomeatal complex, folding the uncinate over the ethmoidal infundibulum and compressing the drainage space for the paranasal sinuses, thereby predisposing a.m. *Homo sapiens* to chronic sinusitis. Aspiration and acute airway obstruction are also a consequence of the laryngeal descent.

It is interesting to speculate on the relative fitness evolutionary pressures of bipedalism, binocular vision, locomotion and speech. Bipedalism must have come first. Locomotion contributed throughout. Even today, speed is an asset. Binocular vision is a nice theory, but in reality, does not require a shorter snout. Oral speech occurred late in the evolutionary process, but once it appeared, exhibited high fitness advantage and substantially influenced the final and recent changes in the upper respiratory tract.

The views presented in this paper represent an anatomic perspective. A separate and concurrent series of events must have occurred in the central nervous system and contributed to speech, sleep and obstructive sleep apnea.

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