Obstructive sleep apnea (OSA) is a common disorder among middle-aged adults, affecting approximately 4% of men and 2% of women. Continuous positive airway pressure (CPAP) during sleep is the best available treatment for the majority of patients in addition to appropriate lifestyle interventions. However, some patients may not comply with or respond to CPAP; approximately one-third of all patients initiated on CPAP do not use the treatment at 5 years.

Remmers et al hypothesized that upper airway occlusion in sleep could be countered by activity of the dilators of the upper airway. This hypothesis has been tested by studying the dilator muscles, in particular the genioglossus muscle, by electrically stimulating them using intraoral surface or intramuscular fine wire electrodes. However, it is difficult to adequately stimulate sufficient bulk of the pharyngeal dilator muscles, and such stimulation often disturbs sleep.

Transcutaneous stimulation of the pharyngeal dilators, in particular the genioglossus, may represent an alternative and better-tolerated approach. However, the therapeutic value of transcutaneous electrical stimulation of the genioglossus muscle in patients with obstructive sleep apnea (OSA) to reduce sleep-disordered breathing is unclear.

Methods: Contraction of the genioglossus muscles during transcutaneous stimulation was investigated using ultrasonography in 11 healthy subjects (seven men, mean [SD] age 30 [6] years; BMI, 24.2 [3.5] kg/m²). Esophageal and gastric pressures were measured with balloon catheters, and transesophageal diaphragm electromyogram (EMGdi) was recorded during polysomnography in 11 patients with OSA (eight men, aged 51 [16] years; BMI, 42.0 [9.7] kg/m²) while transcutaneous electrical stimulation of the genioglossus was applied in non-rapid eye movement sleep (stage N2).

Results: Ultrasonography measurements showed a significant increase in tongue diameter during stimulation (sagittal: 10.0% [2.8%]; coronal: 9.4% [3.7%]). The measurements were reproducible and repeatable. In patients with OSA, snoring decreased during stimulation (P < .001) and oxygenation improved (P = .001); the respiratory disturbance index (RDI) fell from 28.1 (26.3) to 10.2 (10.2) events per hour during stimulation (P = .002), returning to 26.6 (26.0) events per hour after stimulation was stopped. Transdiaphragmatic pressure swing decreased from 24.1 (13.5) cm H₂O to 19.7 (7.1) cm H₂O (P = .022), increasing to 24.2 (10.8) cm H₂O afterward, and EMGdi fell from 23.8% max (12.6% max) to 15.7% max (6.4% max) (P < .001), rising to 22.6% max (10.4% max) post stimulation.

Conclusions: Continuous transcutaneous electrical stimulation of the genioglossus muscle reduces ventilatory load and neural respiratory drive in patients with OSA. 

Abbreviations: AHI = apnea-hypopnea index; CPAP = continuous positive airway pressure; Ds-t = distance skin-to-tongue surface; EMG = electromyogram; EMGdi = transesophageal diaphragm electromyogram; OSA = obstructive sleep apnea; Pdi = transdiaphragmatic pressure; Pes = esophageal pressure; RDI = respiratory disturbance index; SaO₂ = oxygen saturation.
Miki et al. demonstrated that short periods of transcutaneous electrical stimulation decreased the incidence of episodes of upper airway occlusion in OSA. However, Edmonds et al. found transcutaneous electrical stimulation to be ineffective. We hypothesized that low-current transcutaneous electrical stimulation, applied over a longer period, could result in sufficient contraction of the genioglossus muscle to reduce sleep-disordered breathing in patients with OSA without awakening.

**Materials and Methods**

The first part of the study sought to determine a suitable stimulation frequency and intensity that was tolerable and to evaluate with ultrasonography whether transcutaneous electrical stimulation of the genioglossus achieves an effective muscle contraction. Next, we observed the response to stimulation during sleep and studied whether respiratory effort in OSA was reduced.

We used ultrasonography to investigate whether stimulation responses to transcutaneous stimulation in 11 awake normal subjects, then studied the effect of stimulation on sleep-disordered breathing in 11 subjects with known OSA. Participants were initially addressed following referral from the metabolic clinic at King's College Hospital. Patients were excluded if they had significant comorbidities, particularly lung disease. We did not include patients who had been treated for lung disease such as asthma or obesity-hypoventilation syndrome previously. In addition, we did not recruit from patients with acute illness. Eight of our patients with sleep apnea had diabetes, but this was well controlled at the time of the study. The study was approved by King's College Hospital local research ethics committee (reference number 06/Q0703/224), and each participant gave informed written consent.

### Transcutaneous Electrical Stimulation of Genioglossus

The skin was prepared with alcohol wipes and Nuprep skin gel (D. O. Weaver Co; Aurora, Colorado). Two patches (40 x 40 mm) (Verity Medical Ltd; Uplands, England) were placed halfway between the chin and the angle of the mandible over the submental area (Figs 1A, 1B) to deliver transcutaneous stimulation with a NeuroTrac Sports stimulator (Verity Medical Ltd). Stimulation intensity, at a frequency of 30 Hz for approximately 1 min, was titrated to ensure it was comfortable while the patient was awake. Having established a comfortable level of stimulation, the maximal tolerable level of current was also determined.

#### Ultrasonography of the Genioglossus

Ultrasonography was used to measure the thickness of the tongue muscles with an 8-MHz, 5.6-cm linear probe (Toshiba Medical Systems; Tokyo, Japan). Images were taken in both the sagittal and coronal planes with the probe placed under the mandible (Figs 2A, 2B) (additional information on how these measurements were made is available in e-Appendix 1).

The measurement of the distance skin-to-tongue surface (Ds-t) was taken during electrical stimulation (30 Hz, pulse width 250 μs, current 17.5 [2.9] mA) and immediately after the stimulation device was turned off. The probe was kept in the same position between the two measurements. Each Ds-t was measured by two different observers (J. Steier and J. Seymour, random order) who were blind to each other’s measurements. Subjects were measured on two occasions to assess reproducibility.

#### Respiratory Pressures and Electromyography of the Diaphragm and Other Respiratory Muscles

These measurements were made according to the American Thoracic Society/European Respiratory Society joint statement on respiratory muscle testing and as previously described by others. Additional information is given in e-Appendix 1. Multiple respiratory muscle tests were performed as described elsewhere. Four maneuvers, maximal inspiratory effort against a closed shutter, maximum sniff, inspiration to total lung capacity, and maximum voluntary ventilation, were performed. These have been shown to produce maximal or near-maximal diaphragm activation. The largest rectified signals of the electromyogram (EMG) (root-mean-square of the raw data) acquired during spontaneous breathing were quantified off line (time constant 100 ms) and expressed as percentage of maximum EMG activity as derived from the maximum effort maneuvers. All recordings of EMG were sampled at 2 kHz. EMG data were amplified and filtered with a high-pass 30-Hz filter and an additional low-pass filter of 3 kHz.

#### Overnight Study

Eleven patients with OSA underwent the following measurements in addition to submental electrical stimulation and assessment of comfortable and maximal stimulation levels:

- Daytime fatigue symptoms were assessed by the Epworth Sleepiness Scale.
- Spirometry was performed according to international guidelines. Vital capacity was measured in the sitting and supine position.
- Arterialized earlobe blood was collected into a capillary tube and analyzed (Bayer Rapidlab 248; Diamond Diagnostics; Holliston, Massachusetts).
- Full polysomnography was performed using Alice 5 equipment (Respiriconics; Murrysville, Pennsylvania). Sleep and respiratory events were scored with standard terminology (additional information in e-Appendix 1).

Snoring was recorded with a microphone attached to the skin over the larynx and scored independently by two blinded investigators (J. Seymour and W. D.-C. Man.) by using a semiquantitative scale for analyzing 5-min printouts of the microphone recordings prior to, during, and after stimulation (0 = no snoring, 0.5 = very mild, 1 = mild, 2 = moderate, 3 = severe).

After positioning of the catheters and surface electrodes, the patients underwent respiratory muscle tests and went to bed;
2 min of resting breathing were recorded while being awake and supine, and then lights were turned off (10:00 PM-11:00 PM). Once the patient fell asleep, the NeuroTrac Sports device was activated for 10 min during periods of upper airway occlusion, the earliest starting at 10 min after sleep onset. Current intensity was increased over a minute until the level of comfort, as recorded while awake, was reached. Stimulation was delivered during sleep stage N2 with the patient supine. The occurrence of respiratory events during stimulation, as measured by the respiratory disturbance index (RDI), was compared with the 10-min periods prior to and after stimulation. After a break of at least 1 h, stimulation was repeated to determine current intensity that would cause arousal. Stimulation intensity was slowly increased but kept below the maximum tolerated current, as documented in the initial daytime trial, until eventually an arousal from sleep was induced. This current was noted as the “arousal” intensity.

Analysis and Statistics

Results were further analyzed and plotted using SPSS, version 16 (SPSS; Chicago, Illinois) for Mac OS X (Apple; Cupertino, California) and GraphPad Prism 5.0 (GraphPad Software; San Diego, California). Following testing for normality results are given as mean (SD). A P value < 0.05 was considered significant. A repeated-measures analysis of variance was chosen to compare the results of the stimulation periods overnight to periods prior to and after stimulation, using a post hoc analysis with Bonferroni correction for multiple comparisons. Bland-Altman plots in e-Figures 1 and 2 compare repeatability and reproducibility of the ultrasonography measurements; bias and P values are stated in Table 1.36

Results

Ultrasonography Study

We studied 11 awake subjects with ultrasonography (seven men, aged 30 [6] years; BMI, 24.2 [3.5] kg/m²). The mean current used to stimulate genioglossus was 17.8 (2.9) mA. There was an increase in the Ds-t of 10.0% (2.8%) on the sagittal view and 9.4% (3.7%) on the coronal view, on average (all results of occasion 1 and 2 for observer 1 and 2) (Figs 2A, 2B; Table 1). The results were reproducible between observers and repeatable between occasions, without significant differences between observers or occasions (Table 1). (Additional data on the interoccasion repeatability and interobserver reproducibility are given in e-Figs 1 and 2.)

Sleep Study

We studied 11 patients with OSA (eight men, aged 51 [16] years; BMI, 42.0 [9.7] kg/m²; four ex-smokers, one active smoker, and six never smokers) during sleep (Table 2). Each patient was stimulated for at least 10 min during periods of upper airway occlusion. Two examples of the stimulation periods are given in Figures 3A and 3B. Figure 3A shows a patient in whom a relatively high current was used, whereas Figure 3B indicates the more subtle changes with lower stimulation intensity. The mean current used during the first stimulation period was 10.1 (3.7) mA; the mean current to cause arousal from sleep during any of the succeeding stimulation periods was 14.8 (6.9) mA.

Patients’ lung function and respiratory muscle strength is described in Table 2. (Additional data on individual subjects is provided in e-Tables 1-3.) Pulmonary function tests were borderline for restrictive ventilation disorder and revealed slightly low PaO₂ values. Inspiratory and expiratory muscle strength was normal or near normal.27

Total sleep time was, on average, 313.4 (51.5) min, sleep efficiency was 74.6% (18.9%), and rapid eye movement-sleep time was 16.1% (6.4%) of the total sleep time. Two patients (numbers 1 and 9) had a low sleep efficiency, perhaps due to the invasiveness of the study. The nadir of oxygenation and the mean of the desaturations indicated moderately severe OSA (Table 3).

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Saturation (SaO₂) increased with stimulation (P < .001) and remained higher after stimulation stopped. RDI and apnea-hypopnea index (AHI) decreased significantly during stimulation (P < .002). In six of the 11 patients it was reduced to < 5/h. Inspiratory pressures were significantly diminished with electrical stimulation (esophageal pressure [Pes] and transdiaphragmatic pressure [Pdi], P < .022). Neural respiratory saturation (SaO₂) increased with stimulation (P = .001) and remained higher after stimulation stopped. RDI and apnea-hypopnea index (AHI) decreased significantly during stimulation (P = .002). In six of the 11 patients it was reduced to < 5/h. Inspiratory pressures were significantly diminished with electrical stimulation (esophageal pressure [Pes] and transdiaphragmatic pressure [Pdi], P = .022). Neural respiratory

The results of the initial 10-min period of electrical transcutaneous stimulation during upper airway occlusion when asleep are shown in Table 4. (Additional data on individual subjects are provided in e-Tables 4-8). Snoring was reduced by stimulation (P < .001) and, although slightly higher levels of noise were observed when stimulation was turned off, it remained improved for the following 10 min. Oxygen saturation (SaO₂) increased with stimulation (P = .001) and remained higher after stimulation stopped. RDI and apnea-hypopnea index (AHI) decreased significantly during stimulation (P = .002). In six of the 11 patients it was reduced to < 5/h. Inspiratory pressures were significantly diminished with electrical stimulation (esophageal pressure [Pes] and transdiaphragmatic pressure [Pdi], P = .022). Neural respiratory

Table 1—Results of Ultrasonography Measurements

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Occasion 1</th>
<th>Occasion 2</th>
<th>Mean Difference (Bias), mm</th>
<th>P Value</th>
<th>Observer 1</th>
<th>Observer 2</th>
<th>Mean Difference (Bias), mm</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔDs-t (sagittal)</td>
<td>5.8 (2.0)</td>
<td>6.0 (1.1)</td>
<td>0.15 (0.60)</td>
<td>.692</td>
<td>6.0 (1.8)</td>
<td>5.8 (1.5)</td>
<td>0.01 (2.6)</td>
<td>.733</td>
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<tr>
<td></td>
<td>9.8% (3.2%)</td>
<td>10.3% (2.2%)</td>
<td></td>
<td></td>
<td>10.2% (2.9%)</td>
<td>9.9% (2.5%)</td>
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</tr>
<tr>
<td>ΔDs-t (coronal)</td>
<td>5.4 (2.4)</td>
<td>5.4 (2.0)</td>
<td>0.19 (0.91)</td>
<td>.984</td>
<td>5.5 (2.2)</td>
<td>5.3 (2.2)</td>
<td>−0.20 (1.5)</td>
<td>.823</td>
</tr>
<tr>
<td></td>
<td>9.6% (3.9%)</td>
<td>9.7% (3.7%)</td>
<td></td>
<td></td>
<td>9.8% (3.8%)</td>
<td>9.5% (3.9%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are presented as mean (SD). The results of occasions 1 and 2 are summarized in columns 2 and 3, the bias (occasion 2 – 1) in column 4, and the appropriate P value in column 5. The results of the two observers, the bias (observer 2 – 1), and P value comparing their results are given in the four right columns. An increase of around 10% in the diameter would result in an increase of approximately 21% of the cross-sectional area of the tongue, assuming an ideal fit model of a circle (circle area = πr²). ΔDs-t = change in the distance skin-to-tongue surface between stimulation on and off.
drive transesophageal diaphragm electromyogram (EMGdi[%max]) was reduced during stimulation (P < .001) and returned, along with the RDI, to the levels prior to stimulation when the device was turned off (Fig 3, Table 4). Neural respiratory drive and Pdi during resting breathing, awake and supine, were comparable to levels during stimulation when asleep; Pes deflections remained slightly elevated (Table 4). The EEG revealed an electrical artifact during stimulation, but the first stimulation was at low levels of current and the patients did not arouse from sleep (Fig 3B).

**DISCUSSION**

Transcutaneous electrical stimulation of the genioglossus causes a measurable contraction of the tongue and pharyngeal muscles. This effect is reproducible and can be reliably visualized using ultrasonography. Such stimulation of the genioglossus contracts pharyngeal dilator muscles and reduces ventilatory load and neural drive in patients with OSA. Low-current transcutaneous electrical stimulation can be effectively delivered intermittently overnight at levels that do not cause awakening. Overall, respiratory effort and neural respiratory drive during stimulation periods reached levels similar to those during unoccluded breathing while being awake and supine.

**Clinical Significance of Findings**

Given the increasing number of patients diagnosed with OSA and the observed adherence with CPAP, an alternative approach to treatment could be useful. The reduction in obstructive respiratory events in this study suggests that transcutaneous electrical stimulation of the genioglossus has potential as an additional therapy in OSA. We acknowledge that those studied are a selected group of patients and a prospective randomized controlled trial is necessary to determine the usefulness of this approach.

Oliven et al stated electrical stimulation of the genioglossus, using fine wire electrodes that were inserted intraorally into the muscle, and measured upper airway caliper and critical occlusion pressure. Our results are consistent with their findings in that they found around one-half of the tested patients with OSA to have improved pharyngeal patency when stimulated asleep.

Miki et al studied six patients with OSA, placing two silver chloride ECG electrodes, 10 mm in diameter, 1 cm apart on the skin in the submental region. An apnea-triggered stimulator delivered electrical impulses (0.5 milliseconds, 50 Hz) after 5 s of apnea and ceased after airflow resumed or after 10 s. They did not confirm muscle contraction other than by observation. In their study, only two patients were tested with longer periods of stimulation. After initial tests with different stimulation frequencies, we chose a frequency of 30 Hz based on the observation that for all skeletal muscles tension is frequency dependent and stimulation frequencies of 20 to 30 Hz generate about two-thirds of maximum tension, which is well maintained for prolonged periods, whereas prolonged stimulation at 50 Hz is likely to induce fatigue.

A study by Edmonds et al investigated transcutaneous electrical stimulation of the genioglossus in eight patients with OSA, with different findings from those of Miki et al. They found that transcutaneous electrical stimulation during upper airway occlusion was not effective and caused arousal. However, the intensity of stimulation in their study was relatively high. In the present study, the maximal (SD) tolerated current in normal subjects, who were highly motivated and familiar with physiologic studies, was 17.8 (2.9) mA, while being awake, compared with a range of 15 to 39.6 mA used in patients in the study of Edmonds et al. For our overnight stimulation protocol, we used lower currents of 10.1 (3.7) mA, which did not wake the patients (Table 2). It is of interest

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, male:female</td>
<td>8:3</td>
</tr>
<tr>
<td>Age, y</td>
<td>50.7 (15.9)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>42.0 (9.7)</td>
</tr>
<tr>
<td>Neck circumference, cm</td>
<td>43.4 (3.4)</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>1.04 (0.08)</td>
</tr>
<tr>
<td>Epworth Sleepiness Scale Score, points</td>
<td>11.4 (6.4)</td>
</tr>
<tr>
<td>Current/stimulation, mA</td>
<td>10.1 (3.7)</td>
</tr>
<tr>
<td>FEV₁, % predicted</td>
<td>80.8 (15.2)</td>
</tr>
<tr>
<td>VC, % predicted</td>
<td>83.1 (16.3)</td>
</tr>
<tr>
<td>Change in VC, %</td>
<td>4.7 (3.8)</td>
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<tr>
<td>Pco₂, mm Hg</td>
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</tr>
<tr>
<td>PaCO₂, mm Hg</td>
<td>40.5 (3.0)</td>
</tr>
<tr>
<td>Bicarbonate, mmol/L</td>
<td>25.3 (1.4)</td>
</tr>
<tr>
<td>Sniff Pdi, cm H₂O</td>
<td>122.6 (30.7)</td>
</tr>
<tr>
<td>Sniff Pes, cm H₂O</td>
<td>96.7 (23.2)</td>
</tr>
<tr>
<td>Sniff Pnasal, cm H₂O</td>
<td>82.3 (28.2)</td>
</tr>
<tr>
<td>Pmax, cm H₂O</td>
<td>84.8 (28.8)</td>
</tr>
<tr>
<td>PeMax, cm H₂O</td>
<td>133.4 (37.0)</td>
</tr>
<tr>
<td>Cough Pgas, cm H₂O</td>
<td>230.8 (33.8)</td>
</tr>
</tbody>
</table>

All but the cough Pgas and PeMax test results were performed from functional residual capacity. Pmax maneuvers were performed from total lung capacity. Current stimulation: delivered over the initial 10-min period, judged as comfortable while awake. Current arousal: stimulation intensity at which arousal occurred during the second period of stimulation. Change in VC: when changing posture from sitting to supine. VC, % predicted: total lung capacity. Current stimulation: delivered over the initial 10-min period, judged as comfortable while awake. Current arousal: stimulation intensity at which arousal occurred during the second period of stimulation. Change in VC: when changing posture from sitting to supine. VC, % predicted: total lung capacity.

![Table 2—Patient Characteristics, Pulmonary Function Tests, Earlobe Blood Gas Levels, Stimulation Intensity, and Respiratory Muscle Tests](http://journal.publications.chestnet.org/ on 09/01/2015)
that when the stimulation intensity was increased the patients were aroused from sleep at 14.8 (6.9) mA, the lower end of the range of stimulation intensities used by Edmonds et al. It may also be important that we used relatively large pads (40 mm × 40 mm) that allow stimulation of a greater muscle mass, at lower intensity, and therefore less discomfort.

Limitations to This Study

This study did not have a control group. However, we have previously published data on neural respiratory drive and inspiratory pressures in patients with obesity supine and awake. These data are comparable to the levels of drive and inspiratory pressures that we have observed in this trial during electrical stimulation (Table 4). EMGdi supine in obese subjects was 24.7 (8.2) % max, Pes swings were 16.0 (5.0) cm H₂O, and Pdi swings were 18.2 (4.5) cm H₂O.

Transcutaneous electrical stimulation of genioglossus has clear limitations, and there are a number of unknowns when using the technique. Stimulation frequency, wave-form, ramp profile during initiation of stimulation, current intensity, and duration of stimulation need to be more fully investigated. The stimulation is nonspecific, stimulating several pharyngeal, facial, and neck muscles and nerves. Stimulation can sometimes be uncomfortable. These confounders can lead to arousals from sleep.

It could, therefore, be argued that patients woke up during stimulation and that this explains the improvement in the RDI. However, the patients did not have upper airway obstruction when supine and awake at the start of the study, and the flow signal and abdominal and chest wall movements indicated continuing obstructive apneas, of reduced extent, during stimulation. The microphone continued to record some snoring. Inspiratory pressure measurements and the diaphragm EMG demonstrated inspiratory effort that was greater than when awake. SaO₂ demonstrated inspiratory effort that was greater than when awake. Inspiratory pressure measurements and the diaphragm EMG demonstrated inspiratory effort that was greater than when awake. Snoring became more continuous because of permanent airflow, and desaturations were less severe. A stimulation artifact can be observed in the EEG, which could potentially mask arousal from sleep. It is also displayed in the unfiltered raw data of the EMGdi, despite using digital filters, and it is therefore necessary to carefully interpret EMGdi results.

Timing of the stimulation may have influenced the outcome, and arousal thresholds may indeed vary throughout the night. Therefore, our findings may have been influenced by the time chosen to deliver the stimulation. We have tried to deliver the stimulation in all participants as early as possible in the night, closer to sleep onset than to awakening, and arousal threshold at that time may have been higher than it would have been during early morning hours.

Two of the patients had low sleep efficiency. Although this may be caused by the invasive nature of the tests performed, it cannot be ruled out that this is due to disturbance by the stimulation, with intermittent arousal causing an underestimation of the AHI.

Frequently, patients with sleep apnea have more severe sleep-disordered breathing when supine. Therefore, nonsupine posture may alleviate upper airway obstruction and potentially have an impact on therapeutic methods. Hypothetically, stimulation in the nonsupine posture may achieve the same effect at lower levels than in supine posture, but this remains to be tested.

In this study, the investigators manually turned the electrical stimulation on and off. Future studies could focus on automatic devices that could potentially be developed for domiciliary settings. Feedback mechanisms to activate the device might be best based on flow signals to treat sleep apnea and snoring, and this technique might also be used to reduce the burden of nocturnal domiciliary noise. Following the initial experience in this feasibility study we believe that a sham controlled study of patients with sleep apnea using transcutaneous electrical stimulation of the genioglossus throughout the whole of the night in comparison with a control night without stimulation, randomly assigned, is needed to assess benefit from this technique.

Figure 3. A, Transcutaneous stimulation of the genioglossus (stimulation sequence: off-on/off-on; 18 mA) in a patient with repetitive upper airway obstruction in sleep, shown are beginning and end of a 10-min stimulation sequence. Black bars indicate the stimulation artifact in the surface EMG signals. This patient had severe obstructive sleep apnea; there was substantial improvement during electrical stimulation. The inspiratory pressures (Pes, Pdi, both in cm H₂O) decreased, whereas there was still some upper airway obstruction during the initial period as the current was slowly increased. Abdomen and thorax indicate uncalibrated respiratory inductance plethysmography. B, Low-current stimulation in a patient with obstructive sleep apnea, beginning with 1 mA and slowly titrating up to 4 mA. A clear stimulation artifact, increasing with each upward step of current intensity, can be seen in the electromyogram of the sternocleidomastoid (EMGneck). Pes swings and neural respiratory drive decreased; there was continuous airflow with stimulation. Snoring became more continuous because of permanent airflow, and desaturations were less severe. A stimulation artifact can be observed in the EEG, which could potentially mask arousal from sleep. It is also displayed in the unfiltered raw data of the EMGdi, and may have interfered with data analysis, although this signal was processed using digital filters. EMG = electromyogram; EMGdi5 = genioglossus surface electromyogram; EMGdi = the maximum recording of transesophageal electromyogram of the diaphragm; EMGneck = sternocleidomastoid surface electromyogram; Pdi = transdiaphragmatic pressure; Pes = esophageal pressure; Pgas = gastric pressure; SaO₂ = oxygen saturation.

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Original Research
mately 50% to 60% for partial or complete resolution of obstructive episodes, depending on the definition of complete and partial response. Randomized controlled trials indicate that around 35% to 40% of patients with OSA have treatment failure with oral appliances. Best results are achieved with a custom-made mandibular advancement device. The easy use of such devices with a low risk of adverse events helps to improve the compliance of patients, and they are an important treatment option in patients who are not able to cope with CPAP treatment.

In addition, there are different surgical approaches to the treatment of snoring, upper airways resistance syndrome, and OSA. The most successful surgical approach is the extirpation of hyperplastic polyps and tonsils to establish a wider lumen. Among other surgical interventions are the uvulopalatopharyngoplasty, nasal surgery, and maxillofacial surgery. However, data on outcome for these interventions are

Interestingly, a recent presentation of a feasibility study of hypoglossal nerve stimulation therapy to treat OSA using an implantable device (HGNS; Apnex Medical; St. Paul, Minnesota) showed comparable results to the present study with a reduction in AHI from 49.3 (18.1) to 21.6 (11.7) per h, stimulating throughout the night. The approach of using transcutaneous stimulation could help to identify responders and nonresponders prior to implanting such devices.

Alternatives to CPAP in Sleep Apnea

In addition to CPAP, other options to treat sleep apnea include mandibular jaw advancement (dental appliances) and surgical procedures. Oral appliances need to be worn during sleep to maintain upper airway patency by increasing its diameter and reducing its collapsibility. Their success rate is approximately 50% to 60% for partial or complete resolution of obstructive episodes, depending on the definition of complete and partial response. Randomized controlled trials indicate that around 35% to 40% of patients with OSA have treatment failure with oral appliances. Best results are achieved with a custom-made mandibular advancement device. The easy use of such devices with a low risk of adverse events helps to improve the compliance of patients, and they are an important treatment option in patients who are not able to cope with CPAP treatment.

In addition, there are different surgical approaches to the treatment of snoring, upper airways resistance syndrome, and OSA. The most successful surgical approach is the extirpation of hyperplastic polyps and tonsils to establish a wider lumen. Among other surgical interventions are the uvulopalatopharyngoplasty, nasal surgery, and maxillofacial surgery. However, data on outcome for these interventions are

### Table 3—Polysomnography Data

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>TST, min</th>
<th>REM, min</th>
<th>Sleep Efficiency, %</th>
<th>Min SatO₂, %</th>
<th>Mean SatO₂, Desaturation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>146.0</td>
<td>25.0</td>
<td>61.9</td>
<td>97</td>
<td>89</td>
</tr>
<tr>
<td>2</td>
<td>274.0</td>
<td>47.5</td>
<td>72.9</td>
<td>80</td>
<td>85</td>
</tr>
<tr>
<td>3</td>
<td>380.5</td>
<td>73.5</td>
<td>88.5</td>
<td>67</td>
<td>89</td>
</tr>
<tr>
<td>4</td>
<td>302.0</td>
<td>71.5</td>
<td>74.8</td>
<td>78</td>
<td>82</td>
</tr>
<tr>
<td>5</td>
<td>366.5</td>
<td>107.0</td>
<td>87.7</td>
<td>84</td>
<td>88</td>
</tr>
<tr>
<td>6</td>
<td>395.5</td>
<td>50.5</td>
<td>99.9</td>
<td>87</td>
<td>90</td>
</tr>
<tr>
<td>7</td>
<td>389.0</td>
<td>61.5</td>
<td>88.8</td>
<td>72</td>
<td>84</td>
</tr>
<tr>
<td>8</td>
<td>340.0</td>
<td>30.5</td>
<td>70.2</td>
<td>73</td>
<td>83</td>
</tr>
<tr>
<td>9</td>
<td>126.0</td>
<td>10.0</td>
<td>28.0</td>
<td>88</td>
<td>90</td>
</tr>
<tr>
<td>10</td>
<td>314.5</td>
<td>49.0</td>
<td>72.1</td>
<td>88</td>
<td>91</td>
</tr>
<tr>
<td>11</td>
<td>413.0</td>
<td>40.0</td>
<td>75.6</td>
<td>76</td>
<td>80</td>
</tr>
<tr>
<td>Mean</td>
<td>313.36</td>
<td>51.45</td>
<td>74.58</td>
<td>80.00</td>
<td>86.45</td>
</tr>
<tr>
<td>SD</td>
<td>97.50</td>
<td>26.62</td>
<td>18.89</td>
<td>7.38</td>
<td>3.78</td>
</tr>
</tbody>
</table>

REM = rapid eye movement time; SatO₂ = oxygen saturation; TST = total sleep time.

### Table 4—Parameters Awake and Asleep Prior to, During, and After Stimulation

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Awake</th>
<th>10 min Prestimulation</th>
<th>10 min During Stimulation</th>
<th>10 min Poststimulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, beats/min</td>
<td>84 (26)</td>
<td>79 (22)</td>
<td>69 (18)</td>
<td>74 (20)</td>
</tr>
<tr>
<td>Snoring score, 0-3 points</td>
<td>...</td>
<td>2.1 (0.9)</td>
<td>1.4 (0.9)</td>
<td>1.7 (0.9)</td>
</tr>
<tr>
<td>SatO₂, %</td>
<td>...</td>
<td>91.9 (2.1)</td>
<td>93.2 (1.8)</td>
<td>92.8 (2.1)</td>
</tr>
<tr>
<td>RDI, events/h</td>
<td>...</td>
<td>28.1 (26.3)</td>
<td>10.2 (10.2)</td>
<td>26.6 (26.0)</td>
</tr>
<tr>
<td>AHI, per h</td>
<td>...</td>
<td>26.3 (25.1)</td>
<td>10.0 (9.8)</td>
<td>25.7 (25.1)</td>
</tr>
<tr>
<td>Pes, cm H₂O</td>
<td>14.3 (6.1)</td>
<td>23.6 (14.1)</td>
<td>18.3 (7.5)</td>
<td>23.4 (11.3)</td>
</tr>
<tr>
<td>Pdi, cm H₂O</td>
<td>18.7 (6.2)</td>
<td>24.1 (13.5)</td>
<td>19.7 (7.1)</td>
<td>24.2 (10.8)</td>
</tr>
<tr>
<td>EMGdi, μV</td>
<td>25.5 (8.4)</td>
<td>42.9 (30.5)</td>
<td>26.3 (13.4)</td>
<td>40.8 (25.7)</td>
</tr>
<tr>
<td>EMGdi, %max</td>
<td>15.0 (4.4)</td>
<td>23.8 (12.6)</td>
<td>15.7 (6.4)</td>
<td>22.6 (10.4)</td>
</tr>
<tr>
<td>Current, mA</td>
<td>...</td>
<td>10.1 (3.7)</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

Indicated are the differences between awake and stimulation, prior to and during stimulation, and prior to and poststimulation. EMGdi and Pdi normalized to levels during wakefulness; only Pes remained elevated during stimulation. There was a significant reduction of snoring (semiquantitative scale; points) during and after stimulation. SatO₂ improved during and after stimulation. The RDI was reduced with stimulation, compared with both prior to and after, and inspiratory pressures (Pes, Pdi) decreased during electrical stimulation. The EMGdi indicated a decrease in neural respiratory drive during stimulation. AHI = apnea-hypopnea index; EMGdi = transesophageal diaphragm electromyogram; Pdi = transdiaphragmatic pressure; Pes = esophageal pressure; RDI = respiratory disturbance index.

*P < .001.

*P < .01.

*P < .05.
limited in terms of quantifiable impact on physiologic parameters or long-term results, whereas such information is available for CPAP treatment. Registers and careful follow-up are recommended by critical reviewers in this field.47

In this context, the current technique may be used in a cascade of therapeutic options to offer alternative support in the sleep laboratory to patients unable or unwilling to use CPAP. Our data indicate that some patients are more likely to benefit from this technique (six out of the 11 patients had a reduction of RDI below 5/h). We, therefore, think that this technique may be more successful in patients with mild to moderate disease and lower body mass.

Conclusion

In normal awake subjects, transcutaneous electrical stimulation causes contraction of the tongue muscles. In patients with OSA, snoring and sleep-disordered breathing can be improved by continuous stimulation if low current is used to avoid awakening from sleep. The feasibility and effectiveness of low-current transcutaneous genioglossus stimulation requires larger studies, alongside experimental work to determine optimal stimulation paradigms and the development of automated feedback systems.

Acknowledgments

Author contributions: Dr Steier contributed to study design, recruitment, data acquisition, statistical analysis, and manuscript writing. Dr Seymour contributed to study design, recruitment, data acquisition, data analysis, and manuscript writing. Dr Rafferty contributed to study design, statistical analysis, and manuscript writing. Dr Jolley contributed to study design, recruitment, data analysis, and manuscript writing. Dr Man contributed to study design, data acquisition, and manuscript writing. Dr Luo contributed to study design, recruitment, data acquisition, and manuscript writing. Dr Polkey contributed to study design, recruitment, statistical analysis, manuscript writing, and revision. Dr Moxham contributed to study design, recruitment, statistical analysis, manuscript writing, and revision.

Financial/nonfinancial disclosures: The authors have reported to CHEST the following conflicts of interest: Dr Luo has developed the multipair catheter used for the measurement of the diaphragm EMG; no patent is pending. Drs Steier, Seymour, Rafferty, Jolley, Man, Polkey, and Moxham and Mr Solomon have reported that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

Role of sponsors: The sponsor had no influence on the study design, recruitment, analysis, or manuscript writing. The funding was provided to promote independent translational research creating potentially new approaches for treatment.

Additional information: The e-Appendices, e-Figures, and e-Tables can be found in the Online Supplement at http://chestjournal.chestpubs.org/content/140/4/998/suppl/DC1.

References


