Alternative Treatment Options in Mild OSA: Daytime Upper Airway Stimulation ?

18 Annual Pulmonary, Critical Care and Sleep Medicine Update
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Objectives

1. Understand the spectrum and role of upper airway in the pathogenesis of OSA

2. Treatment options for OSA

2. Neuromuscular upper airway stimulation

Spectrum of Sleep Apnea

- Snoring 80% patients with OSA snore
- Hypopnea- partial airflow obstruction with arousal or desaturation 3%-4%
- Apneas- complete airflow obstruction +/- arousal or desaturation

Severity of Sleep Apnea

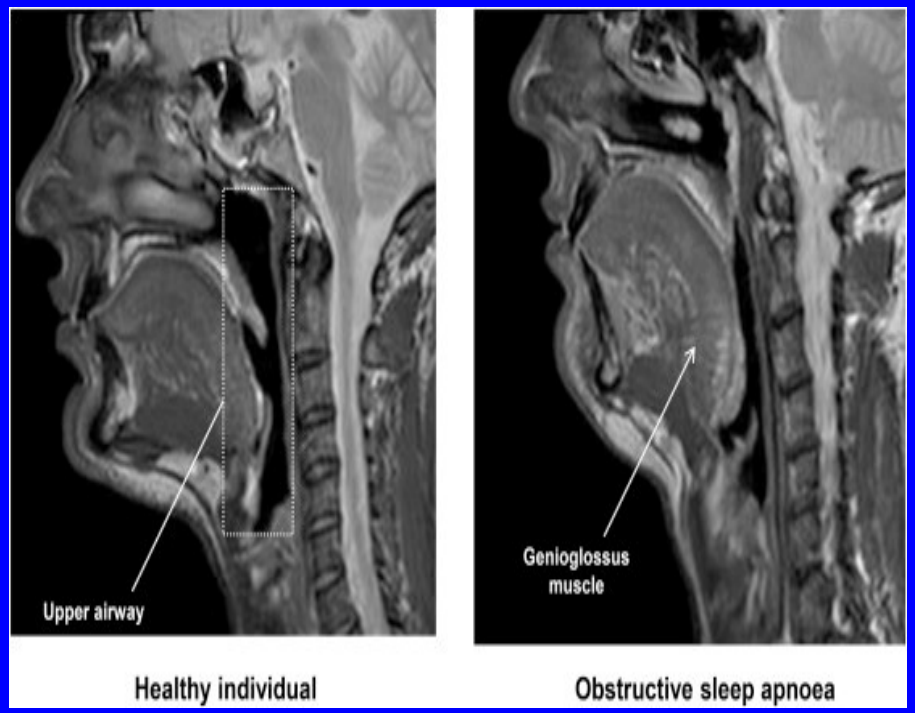
- Apnea Hypopnea Index (AHI): A+H/ sleep hrs
- Respiratory Disturbance Index (RDI): A+H+RERA/ sleep hrs
- AHI or RDI

5-15	Mild	50-55%
15-30	Moderate	25-30%
> 30	Severe	15-20%

- Extent of oxygen desaturation

Role of Upper Airway in Pathogenesis of Obstructive Sleep Apnea

- Site of obstruction: collapsible pharyngeal airway
- Anatomical: Tonsils
  Large tongue
  Retrognathia
- Decreased Muscle tone in sleep
- Decreased arousal responses in sleep



Upper Airway: Dynamic Changes

- Pharyngeal airway- not supported by bony structure
- Genioglossus muscle plays major role

  Anatomic/functional obstruction is overcome by increased activation of the genioglossal muscle in awake state
- Factors impacting dynamic changes:

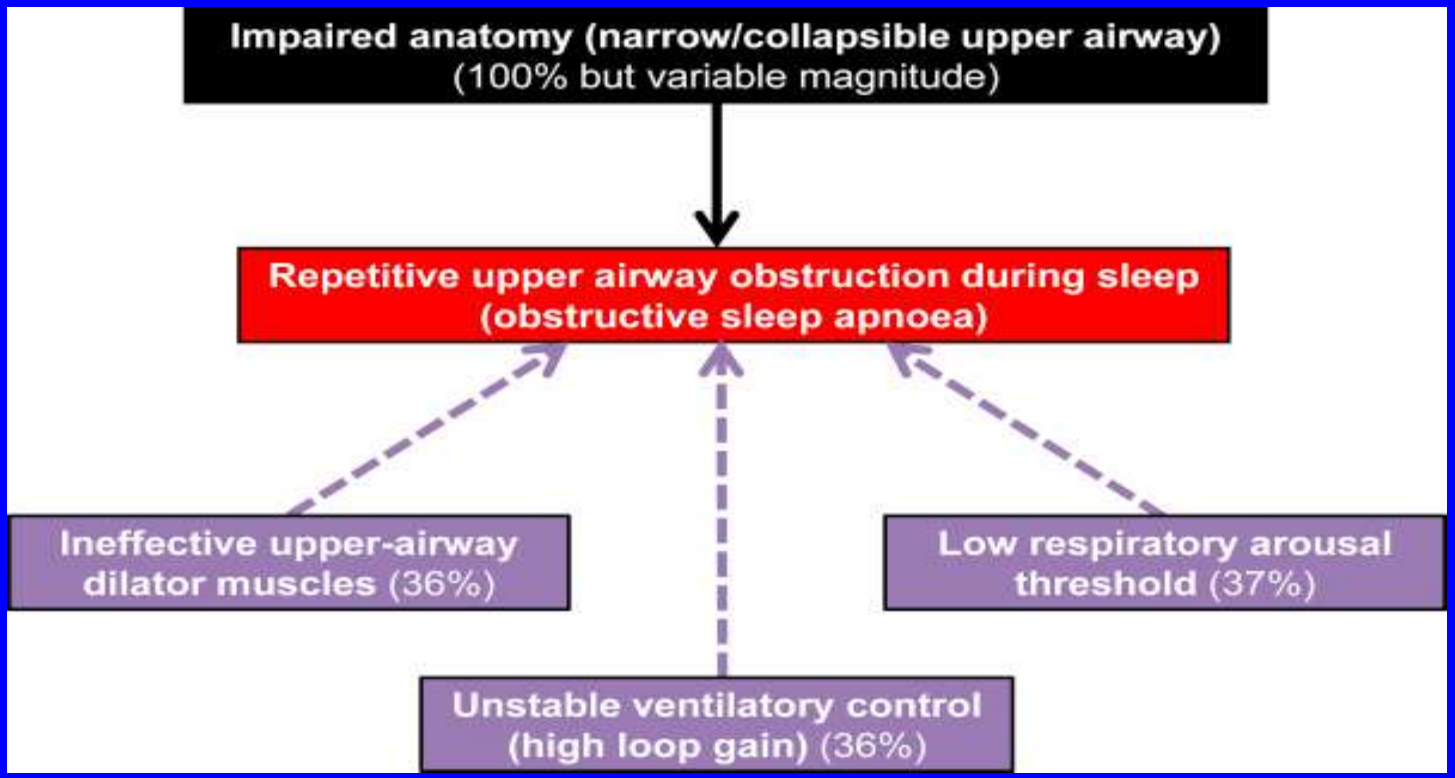
  Length, lung volume, position and airway size

  Fluid shifts in supine position affect airway size

  GERD impacts airway closure

Different Phenotypes Contributing to OSA

Eckert DJ. Sleep Medicine Review 2018; 37:45-59



Treatment Options for OSA

Enlarge Space

- Wt Loss
- CPAP
- EPAP Device
- Mandibular Advancement Device

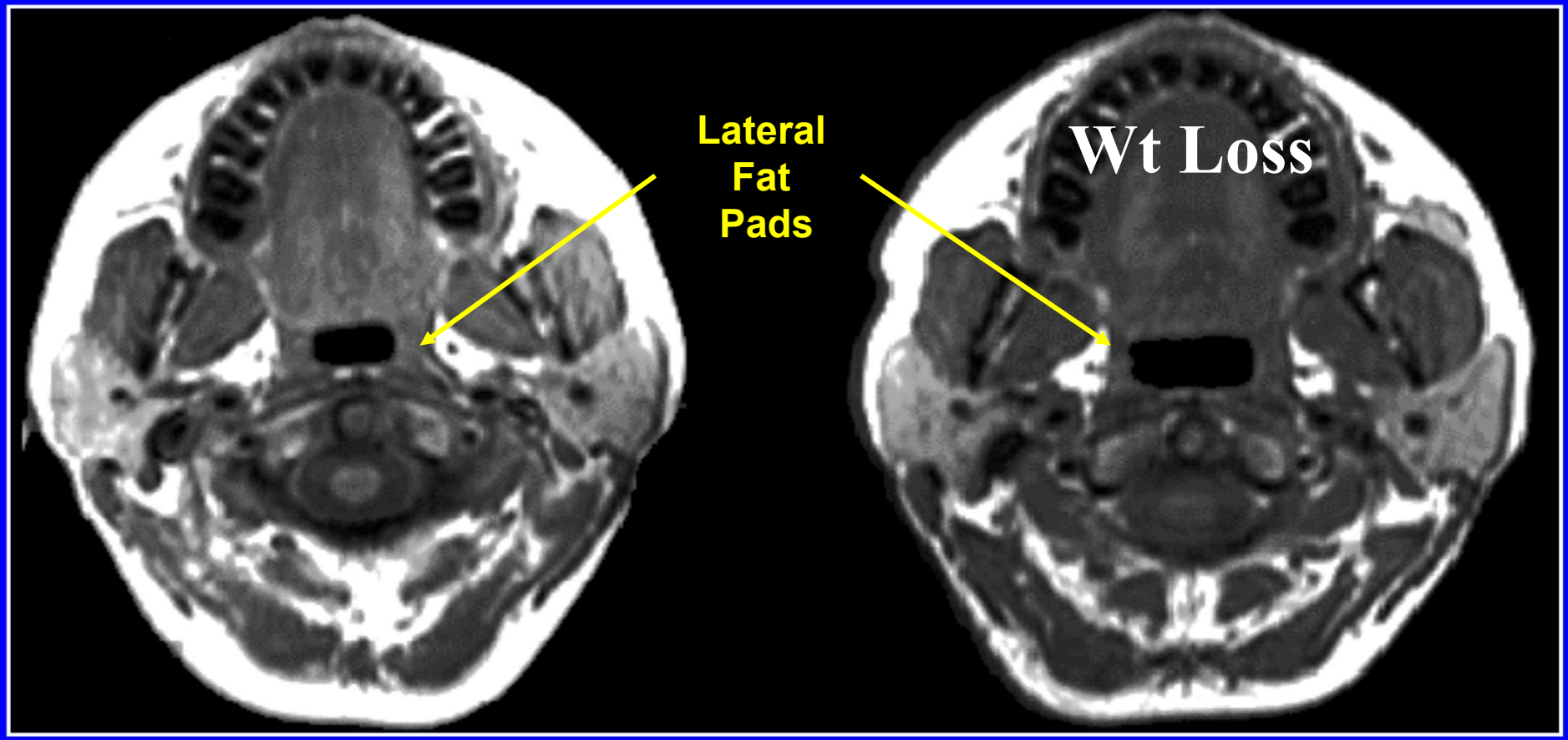
Collapsibility

- Upper Airway Exercises
- Exercise
- Daytime NMES
- Hypoglossal Nerve Stimulation

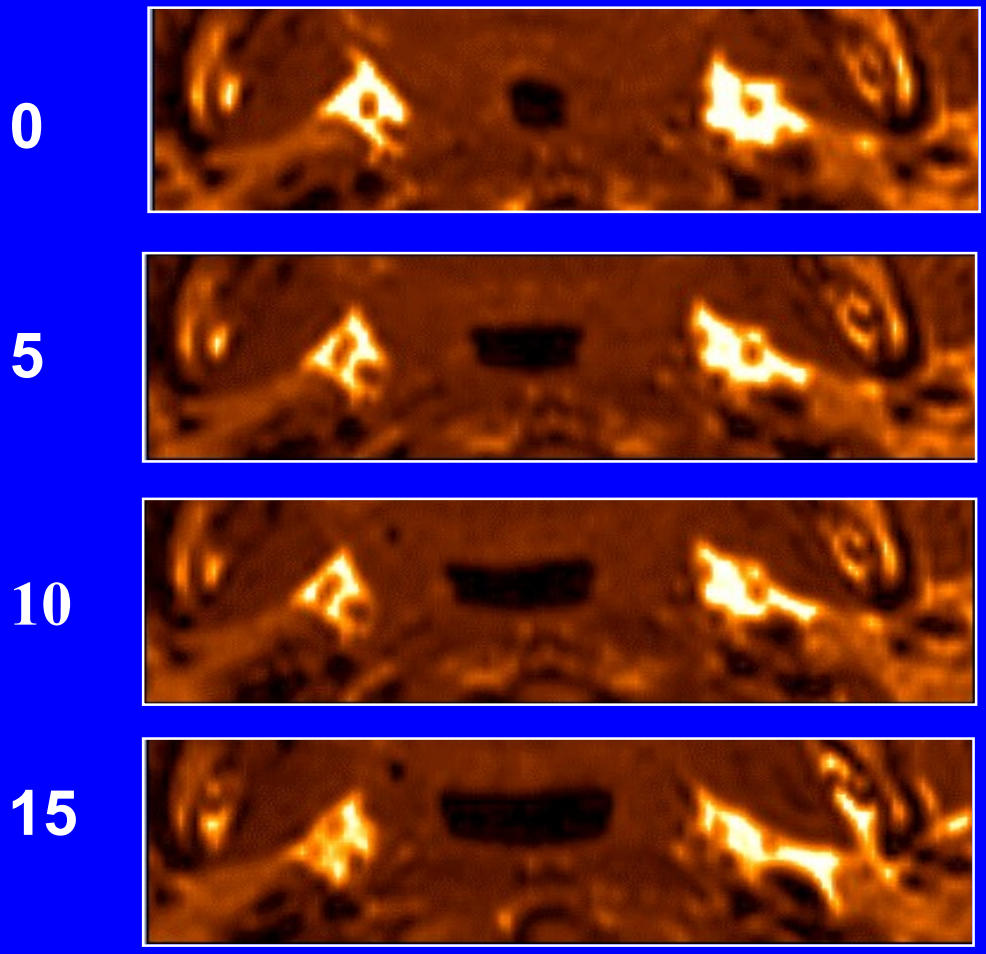
Surgery

- Nasal
- Upper Airway
- Mandibular Osteotomy
- Bariatric Surgery

Obesity and OSAS



CPAP Acts as an Airway Stent and Enlarges Upper Airway Space



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Adjustable Mandibular Advancing Device

- Advances the mandible and tongue forward to enlarge airway space
- AASM: Mild to moderate OSA
- PAP intolerant severe OSA
- Custom fitted
- Follow up PSG critical to document efficacy

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Upper Airway Stimulation For OSA : Inspire Therapy

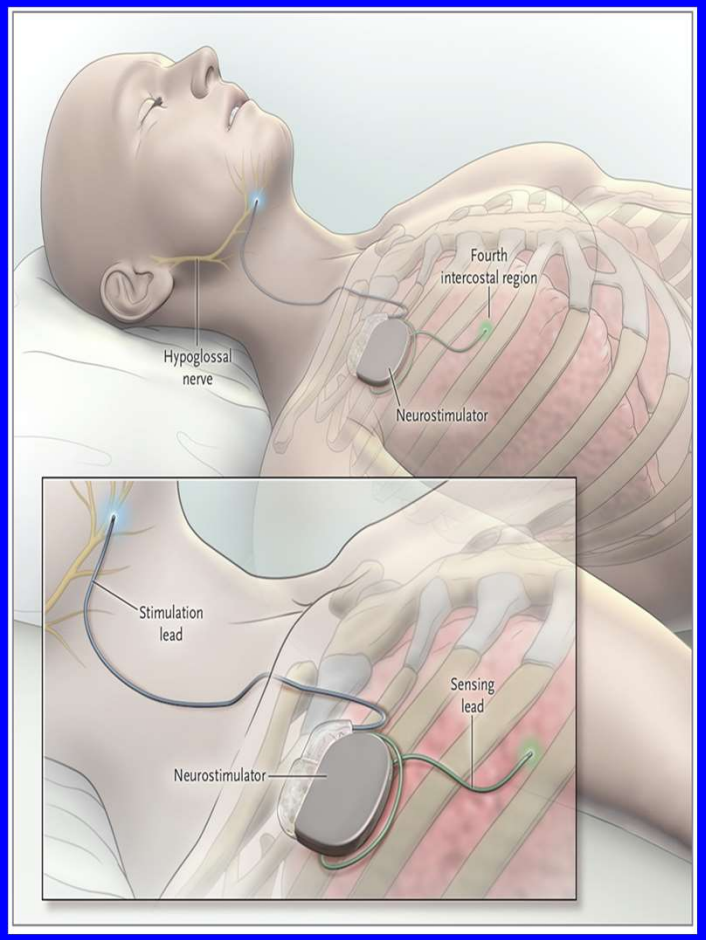
Strollo. NEJM 2014;370: 139-149

- Prospective multicenter, single group study
- CPAP intolerant 126 moderate to severe OSA AHI>15
- Excluded: BMI >32

Concentric airway narrowing on endoscopy

- Primary outcome at 12 months: AHI; ODI

Secondary outcome: ESS, FOSQ

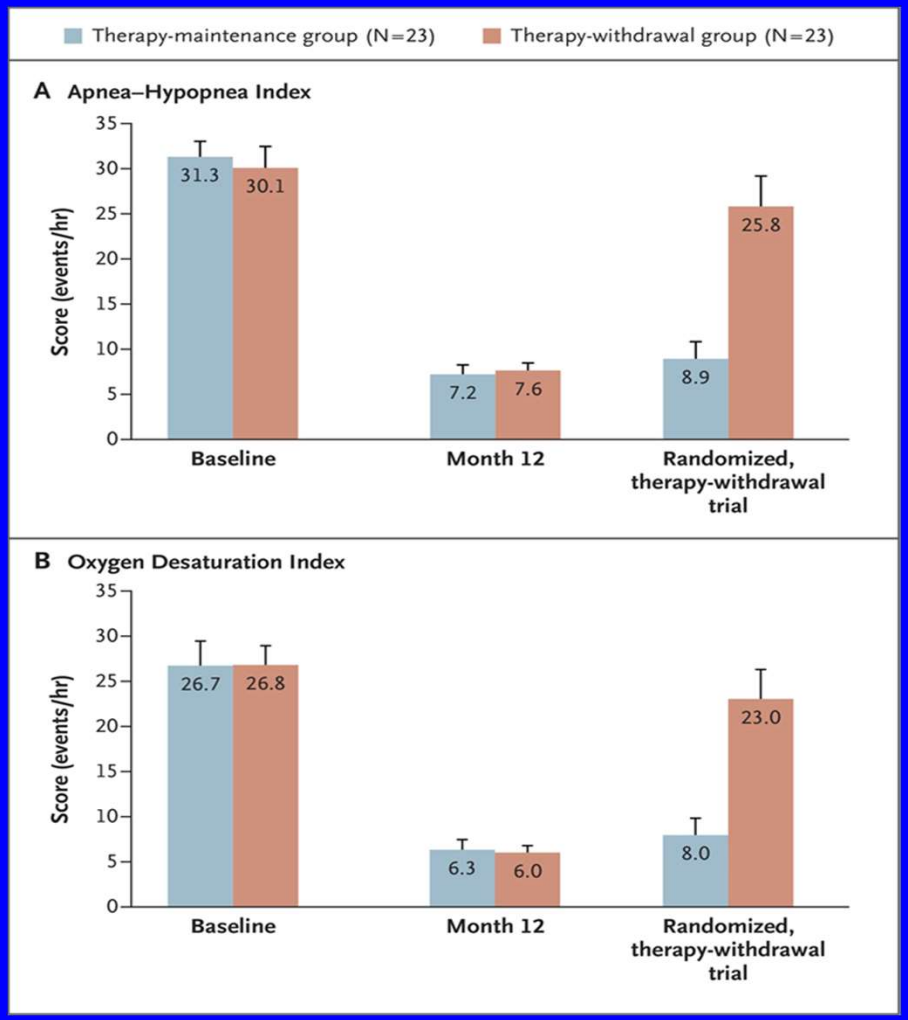


Randomized Therapy Withdrawal Trial at 12 Months

Strollo. NEJM 2014;370: 139-149

Primary Outcomes at 12 Months: AHI and ODI

Randomized therapy withdrawal in 46 consecutive subjects who had good response to therapy



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Playing Didgeridoo Improves OSA

Puhan MA. BMJ, December 23,2005;doi:10.1136/bmj

- 25 patients with mod OSA RCT
- Didgeridoo : 25 min (6days/wk) x 4 months
- EDS, AHI and sleep quality improved significantly in D group as compared to control

Effect of Exercise Training on OSA and Sleep Quality: RCT

Kline CE et al. SLEEP 2011; 34:1631-1640

- 12 week exercise program **(E)** n=27 (mod intensity **AE** 40 min x 4/week +**RT** x 2/week compared to control n=16 (stretching exercise x2/week)
- Modest treatment efficacy with **"E"** with reduction in AHI and ODI and improvement in sleep quality without significant decrease in body weight

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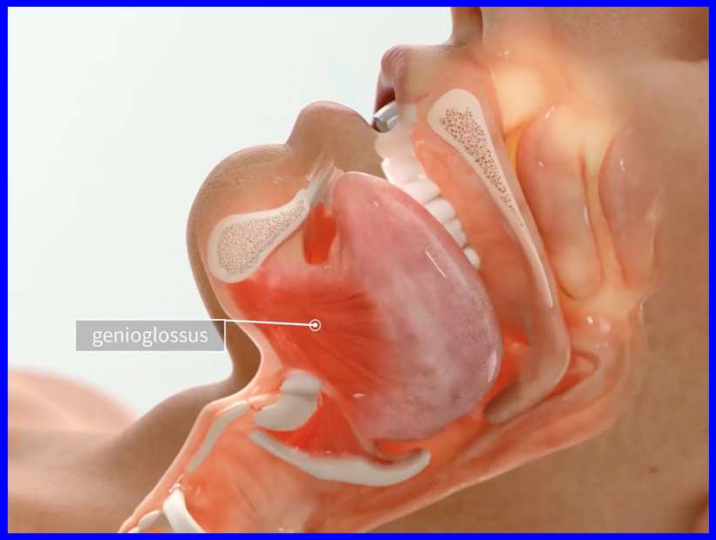
Novel Approach to Training Upper Airway Dilator Muscles to Reduce OSA Severity

Nokes B. Sleep and Breathing May 2022

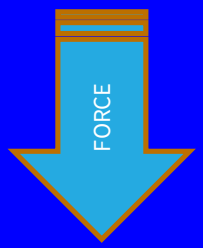
- Innovative approach to provide **daytime** neuromuscular electrical stimulation (NMES)
- Goal: Improve strength and endurance of GG muscle

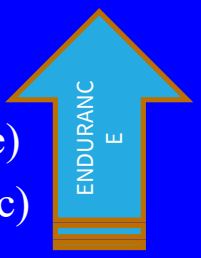
Introduction to eXciteOSA

The role of the genioglossus in OSA pathophysiology



- The largest upper airway muscle is the genioglossus
- The genioglossus is *necessary* and *sufficient* for maintaining upper airway patency[1]
- As in all skeletal muscles, the genioglossus consists of:
  - Type I (slow twitch)
  - Type IIA (fast twitch; oxidative)
  - Type IIB (fast twitch; glycolytic)



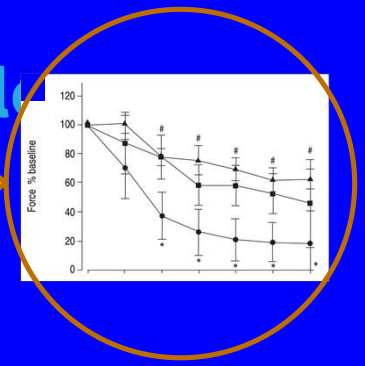


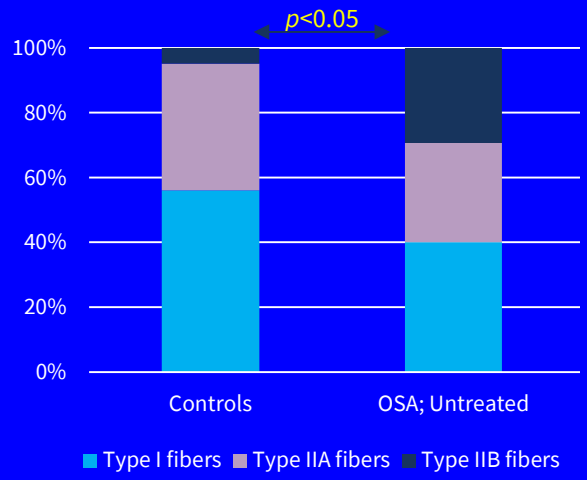
1. Jordan AS, White DP, Lo YL, Wellman A, Eckert DJ, Yim-Yeh S, Eikermann M, Smith SA, Stevenson KE, Malhotra A. Airway dilator muscle activity and lung volume during stable breathing in obstructive sleep apnea. *Sleep* 32(3):361-8 (2009)

Introduction to eXciteOSA

The role of the genioglossus in OSA pathophysiol

- The genioglossus of OSA patients has ↑ Type II and ↓ Type I fibers compared with controls[1,2]
- This corresponds to increased *in vitro* fatiguability of these fibers





1. Carrera M, Barbe F, Sauleda J, Tomas M, Gomez C, Agusti AG. Patients with obstructive sleep apnea exhibit genioglossus dysfunction that is normalized after treatment with continuous positive airway pressure. *Am J Resp Crit Care Med* 159(6):1960-6 (1999)
2. Carrera M, Barbe F, Sauleda J, Tomas M, Gomez C, Santos C, Agusti AG. Effects of obesity upon genioglossus structure and function in obstructive sleep apnoea. *Eur Respir J* 23(3):425-9 (2004)

The clinical experience

Therapy phases

20 minutes a session

1 time each day

6 weeks

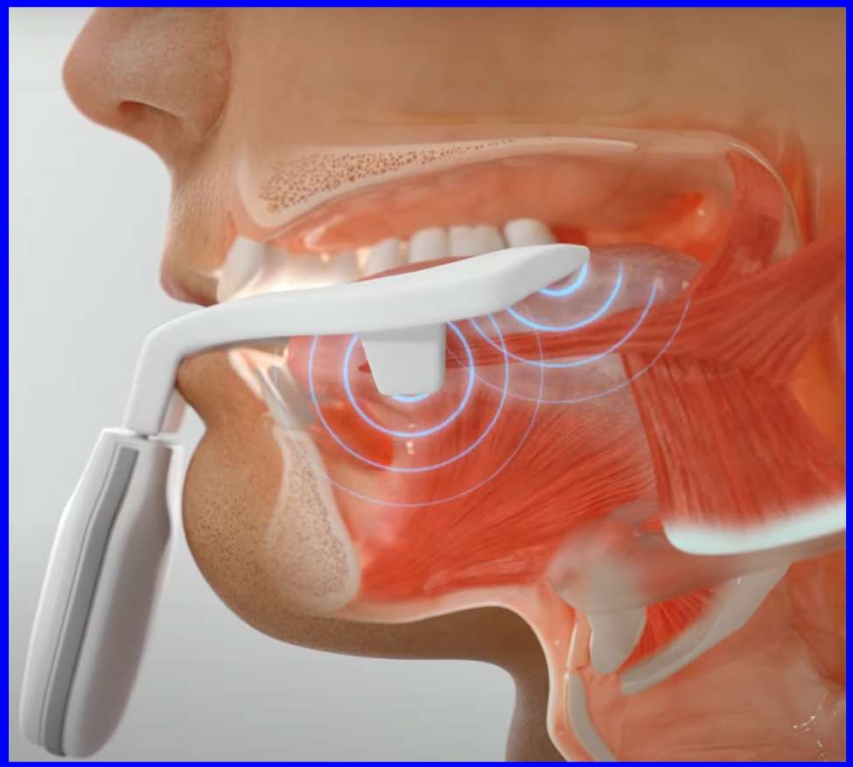
Phase 1

2 times per week *or more*

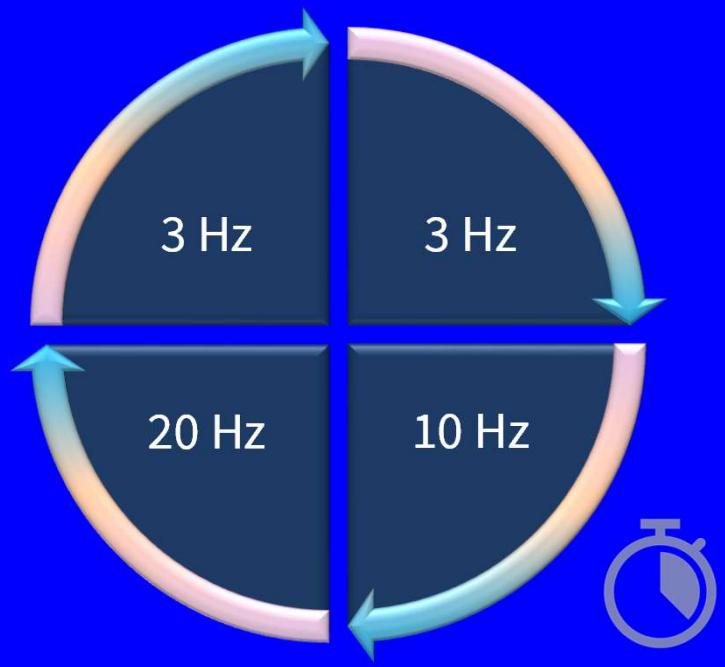
Phase 2

The clinical experience

Stimulation frequencies



Six seconds pulse, four seconds rest



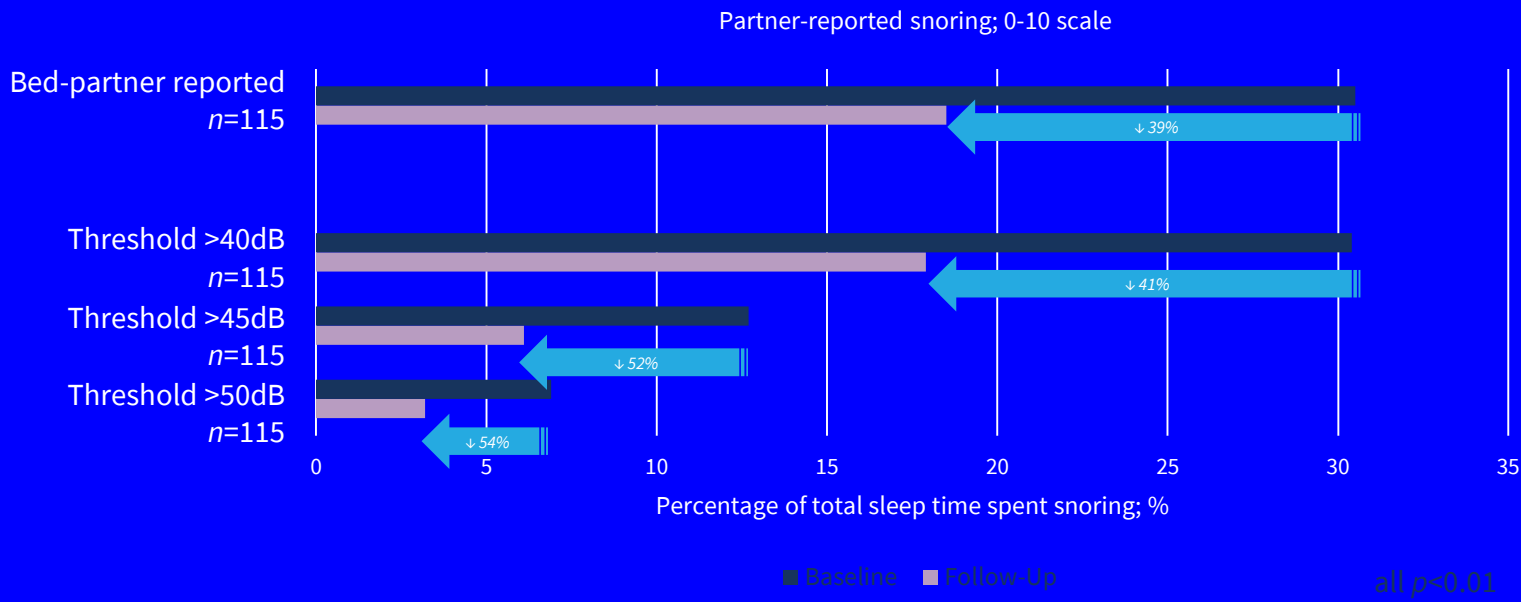
Novel Approach to Training Upper Airway Dilator Muscles to Reduce OSA Severity

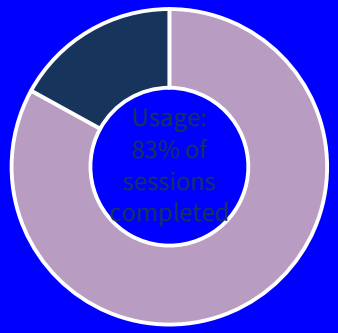
Nokes B. Sleep and Breathing May 2022

- 65 participants (M 68%) with mild OSA (AHI 5-14.9/h) median age 49 years, median BMI 27.7 kg/m2,
- Received NMES for 20 minutes once daily x 6 weeks
- **All patients:** AHI reduced from 10.4/h to 6.8/h
  Responders: AHI reduced from 10.4/h to 5.0/h.
- Statistical improvement in ESS, PSQI and objectively measured snoring and bedpartner reported snoring noted

Overview of clinical trials

Impact of eXcite OSA on snoring





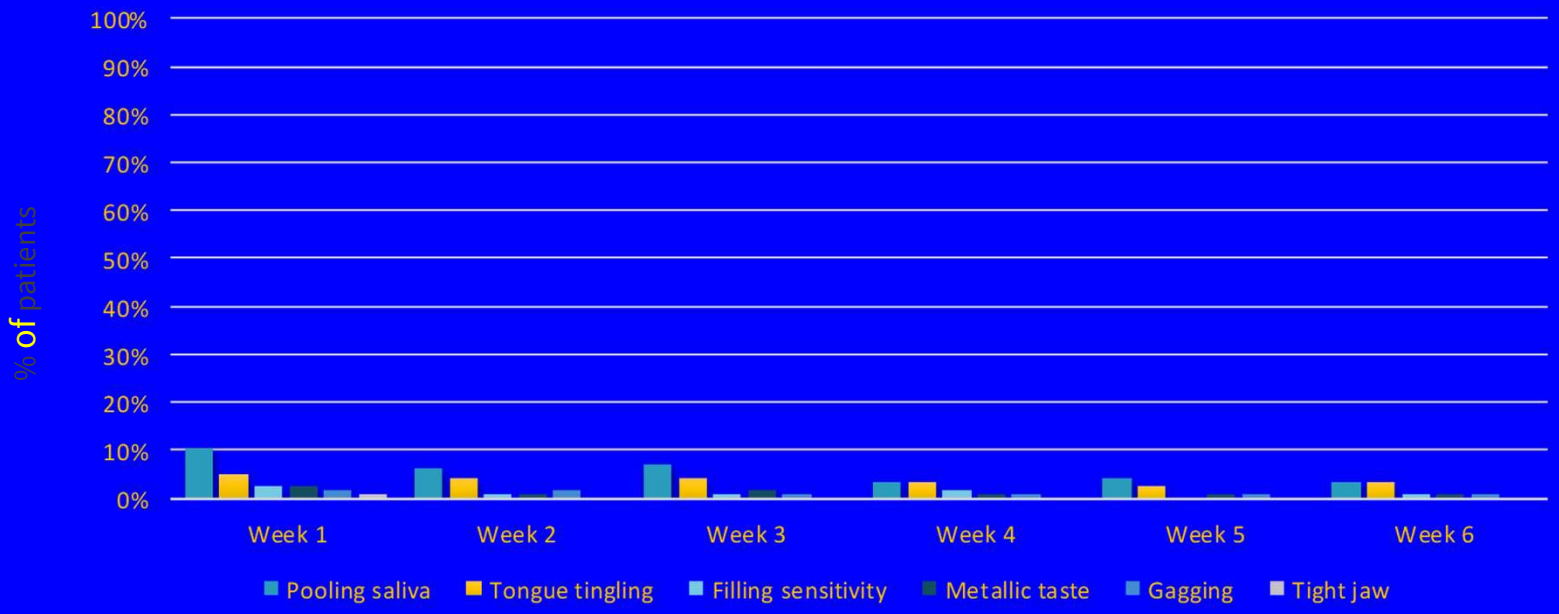
Statistically-significant reductions in bed-partner reported snoring assessed in a two-week diary
Statistically-significant reductions in objectively-measured snoring above thresholds of 40, 45, and 50dB
40dB is the threshold that the WHO uses to define night-time noise pollution[1]

ClinicalTrials.Gov
NCT03829956

1. https://www.euro.who.int/en/health-topics/environment-and-health/noise/policy/who-night-noise-guidelines-for-europe
2. Baptista PM, Martinez Ruiz de Apodaca P, Carrasco M, Fernandez S, Wong PY, Zhang H, Hassaan A, Kotecha B. Daytime neuromuscular electrical therapy of tongue muscles in improving snoring in individuals with primary snoring and mild obstructive sleep apnea. *J Clin Med* 10(9):1-11 (2021)

Overview of clinical trials

Adverse events related to eXciteOSA



No serious adverse events were reported
85% of study participants did not experience any related adverse events
Reported side effects were limited to each 20-minute therapy session, with no ongoing effects

ClinicalTrials.Gov
NCT03829956

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