EVIDENCE BASED OSA MANAGEMENT AND NON-PAP THERAPIES

Atul Malhotra, MD
UC San Diego
Professor of Medicine and Sleep Specialist

Saturday, January 19, 2019 – 8:10 a.m. – 8:50 a.m.

Atul Malhotra, MD, is a board-certified pulmonologist, intensivist and chief of Pulmonary, Critical Care and Sleep Medicine. He is active clinically in pulmonary, critical care and sleep medicine. In the sleep clinic, he provides a full spectrum of diagnostic and therapeutic services to patients with sleep-related disorders, including sleep apnea, insomnia, restless leg syndrome, narcolepsy and sleep disorders associated with medical or psychiatric conditions. He has a special interest in the treatment of sleep apnea.

Dr. Malhotra is the president of the American Thoracic Society. He has taught and presented his research on sleep-related disorders locally, regionally, nationally and internationally. He has published more than 200 original manuscripts in leading journals. He is a principal- and co-investigator on numerous projects relating to sleep apnea and serves as an ad hoc reviewer for many leading journals including the New England Journal of Medicine, Mayo Clinic Proceedings, Sleep and the Journal of American Medical Association. To view a full list of his publications, visit PubMed.

As a professor in the Department of Medicine, Dr. Malhotra is involved in training medical students, residents and fellows at UC San Diego School of Medicine.

Before joining UC San Diego Health, Dr. Malhotra practiced pulmonary, critical care and sleep medicine at Massachusetts General Hospital, Beth Israel Deaconess Medical Center and Brigham and Women's Hospital. He also served as attending physician in intensive care at King Faisal Hospital in Rwanda. He was associate professor at Harvard Medical School and medical director of the Brigham and Women's Hospital Sleep Disorders Research Program.

Dr. Malhotra completed his fellowship training in pulmonary and critical care medicine at Harvard Medical School and a residency in internal medicine at the Mayo Clinic. He completed an internship at St. Thomas Medical Center in Akron, OH and received his medical degree from the University of Alberta in Canada. Dr. Malhotra is triple board-certified in pulmonary disease, sleep medicine and critical care medicine.

Obstructive Sleep Apnea

Evidence Based Treatment

Atul Malhotra, MD

UC San Diego

Previous President ATS

Disclosures: none since 2012; Resmed provided a philanthropic gift to UCSD

Take Home Points

1. CPAP is treatment of choice for OSA and a defeatist attitude about CPAP is not justifiable
2. Alternative therapies are available which provide acceptable results for select patients
3. Individualized therapy may be viable in the future based on mechanism underlying OSA
4. Exciting time for sleep field

ORIGINAL ARTICLE

CPAP for Prevention of Cardiovascular Events in Obstructive Sleep Apnea

R. Doug McEvoy, M.D., Nick A. Antic, M.D., Ph.D., Emma Heeley, Ph.D., Yuanming Luo, M.D., Qiong Ou, M.D., Xilong Zhang, M.D., Olga Mediano, M.D., Rui Chen, M.D., Luciano F. Drager, M.D., Ph.D., Zhihong Liu, M.D., Ph.D., Guofang Chen, M.D., Baoliang Du, M.D., Nigel McArdle, M.D., Sutapa Mukherjee, M.D., Ph.D., Manjari Tripathi, M.D., Laurent Billot, M.Sc., Qiang Li, M.Biostat., Geraldo Lorenzi-Filho, M.D., Ferran Barbe, M.D., Susan Redline, M.D., M.P.H., Jiguang Wang, M.D., Ph.D., Hisatomi Arima, M.D., Ph.D., Bruce Neal, M.D., Ph.D., David P. White, M.D., Ron R. Grunstein, M.D., Ph.D., Nanshan Zhong, M.D., and Craig S. Anderson, M.D., Ph.D., for the SAVE Investigators and Coordinators*

Therapy with CPAP plus usual care, as compared with usual care alone, did not prevent cardiovascular events in patients with moderate-to-severe obstructive sleep apnea and established cardiovascular disease. (Funded by the National Health and Medical Re-

NEJM 2016

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R. Doug McEvoy, M.D., Nick A. Antic, M.D., Ph.D., Emma Heeley, Ph.D., Yuanming Luo, M.D., Qiong Ou, M.D., Xilong Zhang, M.D., Olga Mediano, M.D., Rui Chen, M.D., Luciano F. Drager, M.D., Ph.D., Zhihong Liu, M.D., Ph.D., Guofang Chen, M.D., Baoliang Du, M.D., Nigel McArdle, M.D.,
Sutapa Mukherjee, M.D.,
Qiang Li, M.Biostat.,
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Hisatomi Arima, M.D., P
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NEJM 2016

Need better therapies/adherence
Need to identify high risk patients better
Need more basic research re: mechanisms

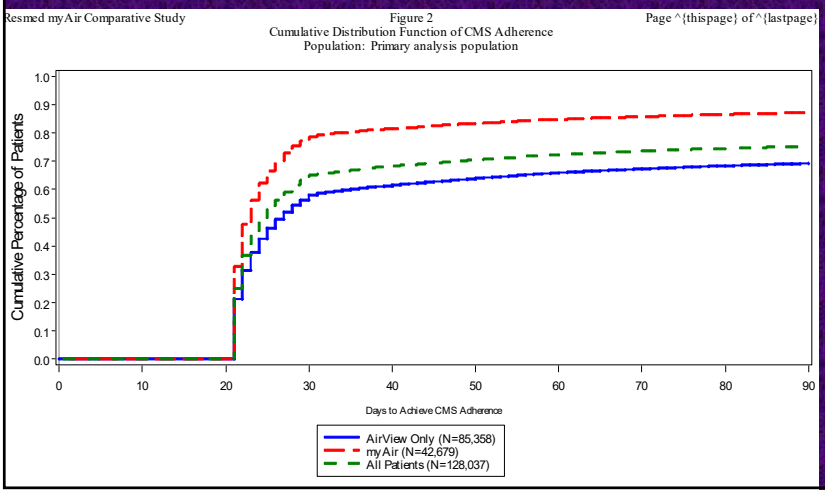
Patient Engagement Using New Technology to Improve Adherence to Positive Airway Pressure Therapy

A Retrospective Analysis

Atul Malhotra, MD; Maureen E. Crocker, BS; Leslee Willes, MS; Colleen Kelly, PhD; Sue Lynch, RN; and Adam V. Benjafield, PhD

Chest 2018

N=952,819 patients with 137,089,667 nights of recording.

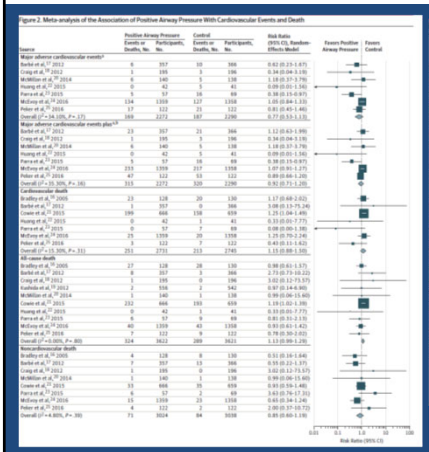


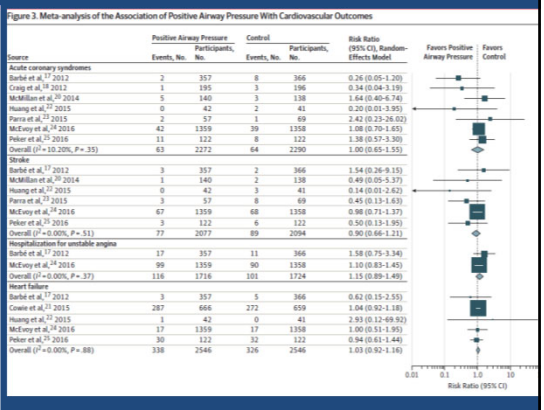
JAMA | Original Investigation

Association of Positive Airway Pressure With Cardiovascular Events and Death in Adults With Sleep Apnea

A Systematic Review and Meta-analysis

Jie Yu, MD; Zien Zhou, MD; R. Doug McEvoy, MD; Craig S. Anderson, PhD; Anthony Rodgers, PhD; Vlado Perkovic, PhD; Bruce Neal, PhD





JAMA 2017

Nasal CPAP is the Treatment of Choice

- Improves symptoms
- Improves blood pressure
- Transformative for some patients

- Need new therapies based on ongoing research

REVIEW ARTICLES

JCSM
Journal of Clinical Sleep Medicine

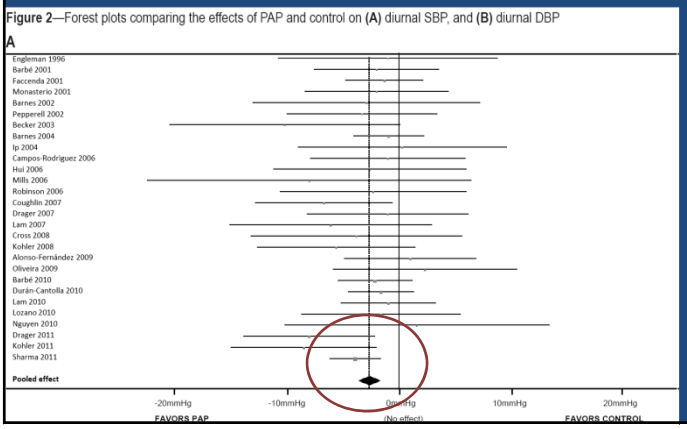
http://dx.doi.org/10.5664/xxxxxxxxxxxxxx

The Effect of Continuous Positive Airway Pressure Treatment on Blood Pressure: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Sydney B. Montesi, M.D.[1,2]; Bradley A. Edwards, Ph.D.[1]; Atul Malhotra, M.D.[1]; Jessie P. Bakker, Ph.D.[1]

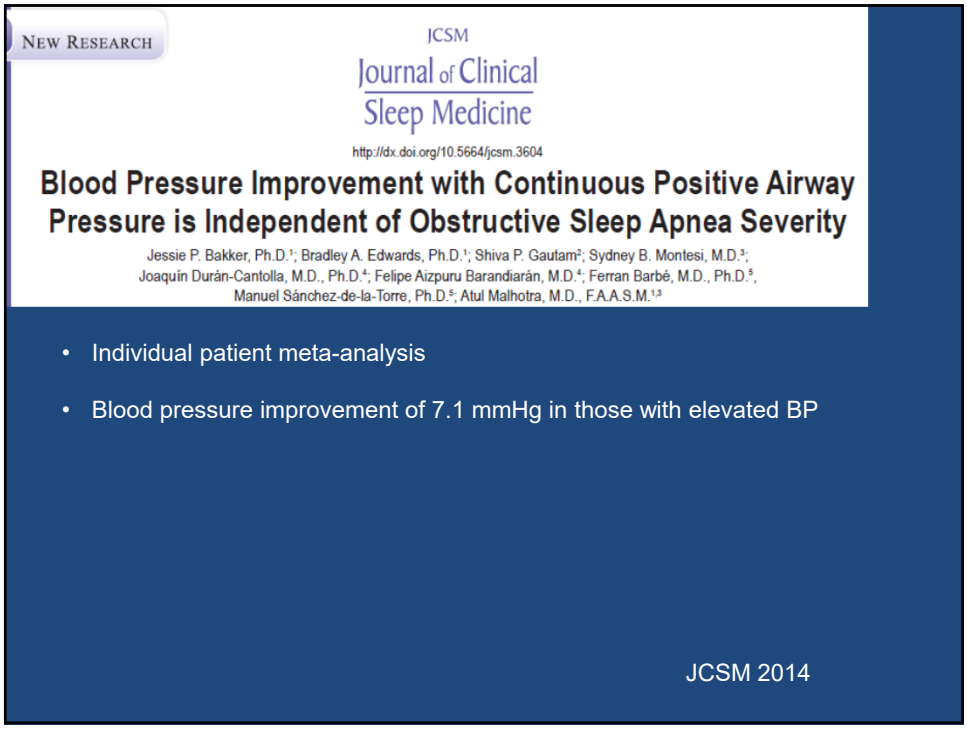
[1]*Sleep Disorders Research Program, Brigham & Women's Hospital & Harvard Medical School, Boston MA;*
[2]*Pulmonary and Critical Care Unit, Massachusetts General Hospital, Boston, MA*

Figure 2—Forest plots comparing the effects of PAP and control on **(A)** diurnal SBP, and **(B)** diurnal DBP



JCSM 2012

Maximum effect in
1. Younger
2. Higher ESS
3. More severe OSA
4. CPAP adherence



- Individual patient meta-analysis
- Blood pressure improvement of 7.1 mmHg in those with elevated BP

JCSM 2014

Modest Blood Pressure Improvement with OSA?

- 1. If your only reason to treat OSA is BP then there is better improvement with valsartan (AJRCCM 2010)
- 2. Some patients get marked improvements in BP
- 3. BP surges are not captured with non-invasive technology and maybe substrate for plaque rupture
- 4. Treatment of OSA helps oxidative stress and other potential causal pathways.
- 5. Adherence is critical for CPAP > other therapies

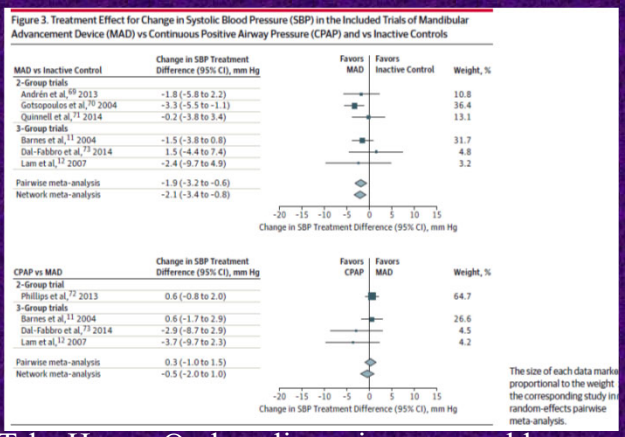
Jordan et al. Lancet 2014; Bhattacharjee et al. in press; Xue et al. AJRCMB 2017

Original Investigation

CPAP vs Mandibular Advancement Devices and Blood Pressure in Patients With Obstructive Sleep Apnea
A Systematic Review and Meta-analysis

Daniel J. Bratton, PhD; Thomas Gaisl, MD; Annette M. Wons, MD; Malcolm Kohler, MD

Figure 3. Treatment Effect for Change in Systolic Blood Pressure (SBP) in the Included Trials of Mandibular Advancement Device (MAD) vs Continuous Positive Airway Pressure (CPAP) and vs Inactive Controls



Take Home: Oral appliance is a reasonable second line option for OSA, particularly mild to moderate

JAMA 2015

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

CPAP versus Oxygen in Obstructive Sleep Apnea

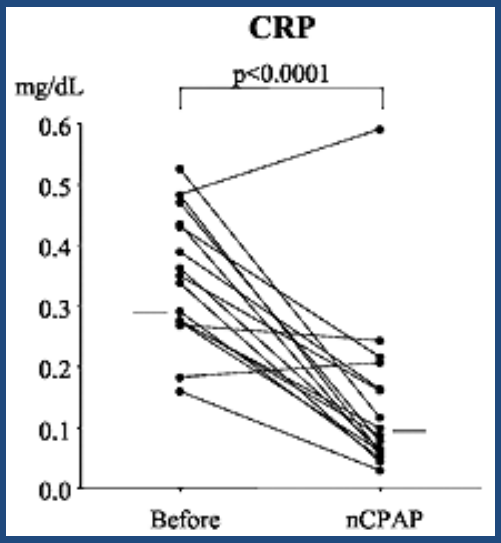
Daniel J. Gottlieb, M.D., M.P.H., Naresh M. Punjabi, M.D., Ph.D., Reena Mehra, M.D., Sanjay R. Patel, M.D., Stuart F. Quan, M.D., Denise C. Babineau, Ph.D., Russell P. Tracy, Ph.D., Michael Rueschman, M.P.H., Roger S. Blumenthal, M.D., Eldrin F. Lewis, M.D., Deepak L. Bhatt, M.D., M.P.H., and Susan Redline. M.D.. M.P.H.

Variable	CPAP (N=90)	NSO (N=94)	HLSE (N=97)	CPAP vs. HLSE	NSO vs. HLSE	CPAP vs. NSO
24-Hr mean arterial blood pressure						
Baseline	89.5±8.6	88.6±10.0	87.7±9.3			
12 Wk	87.8±8.1	90.2±11.1	89.0±11.2	−2.4 (P=0.04)	0.4 (P=0.71)	−2.8 (P=0.02)

NEJM 2014

C-Reactive Protein in Patients with OSA is Reduced by Nasal CPAP

(Yokoe et al., Circulation 107:1129, 2003)

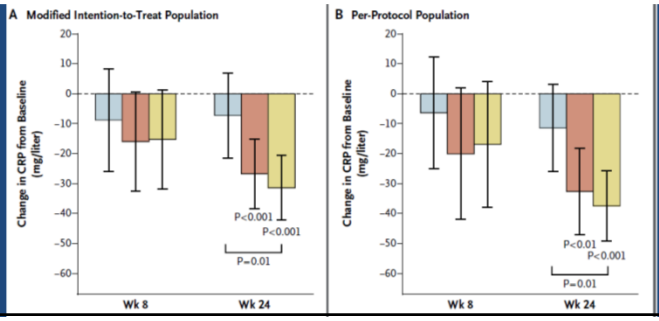


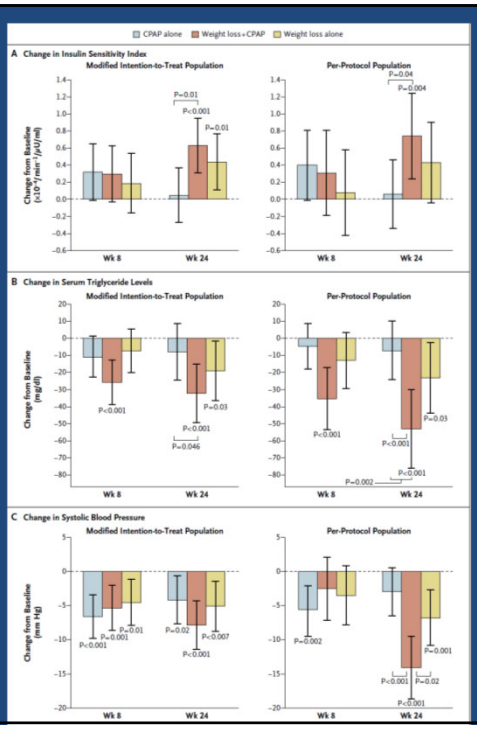
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 12, 2014 VOL. 370 NO. 24

CPAP, Weight Loss, or Both for Obstructive Sleep Apnea

Julio A. Chirinos, M.D., Ph.D., Indira Gurubhagavatula, M.D., Karen Teff, Ph.D., Daniel J. Rader, M.D., Thomas A. Wadden, Ph.D., Raymond Townsend, M.D., Gary D. Foster, Ph.D., Greg Maislin, M.S., M.A., Hassam Saif, M.D., Preston Broderick, M.A., Jesse Chittams, M.S., Alexandra L. Hanlon, Ph.D., and Allan I. Pack, M.B., Ch.B., Ph.D.





JAMA 2012 Sep 19;308(11):1142-9.
Surgical vs conventional therapy for weight loss treatment of obstructive sleep apnea: a randomized controlled trial.
Dixon et al.

N= 60 with BMI 35-55 kg/m2

Conventional led to 5.1 kg vs. 27.8 kg weight loss in lap band (p<0.01)

AHI decrease was 14 vs. 25.5 p=ns

CONCLUSION:
Among a group of obese patients with OSA, the use of bariatric surgery compared with conventional weight loss therapy did not result in a statistically greater reduction in AHI despite major differences in weight loss.

Interpretation: even modest weight loss works

Gastric banding surgery versus CPAP for OSA: The ABC randomized controlled trial

Bakker et al. AJRCCM in press.

N=49 randomized LGB vs. CPAP to examine impact on effective AHI

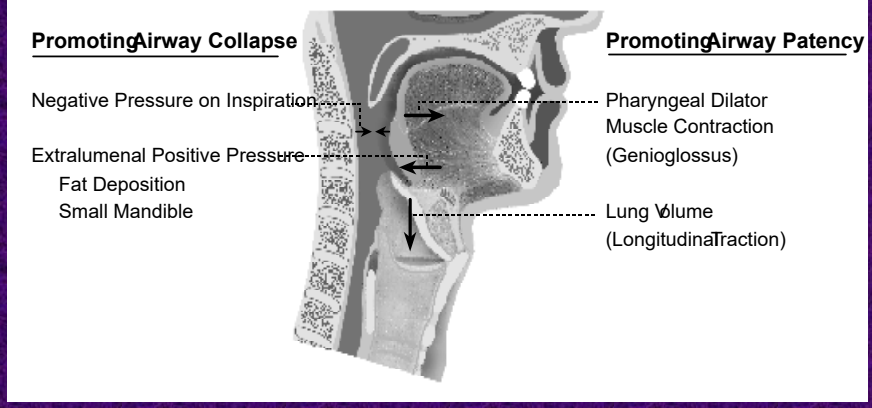
AHI=29.5 vs. 20.0 in LGB vs. CPAP at 9mos and 20.9 vs. 21.4 at 18mos.

No difference in ESS or other important symptoms

These data suggest that OSA patients should not be encouraged to pursue LGB without concurrent CPAP

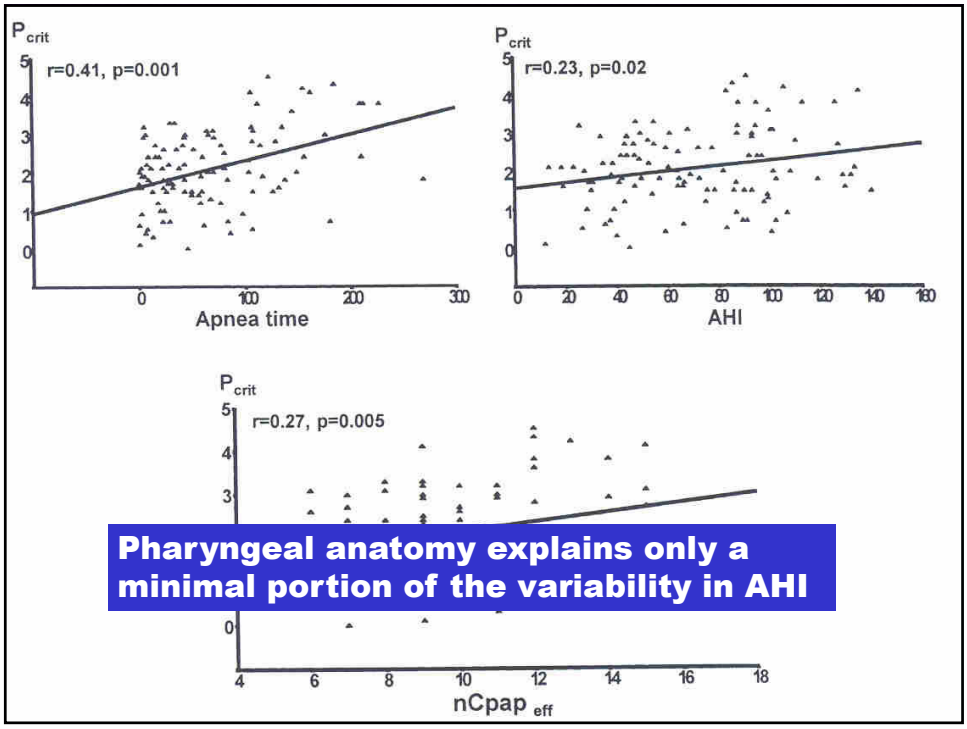
OSA Mechanisms

- **There are likely to be multiple mechanistic pathways which we need to understand and recognize**
- **Patients do not all get OSA for the same reason**



Obstructive Sleep Apnea
Underlying Mechanisms

- Anatomy
- Pharyngeal dilator muscle control asleep
- Arousal Threshold
- Loop gain
- Lung volume
- Vascular



Obstructive Sleep Apnea
Underlying Mechanisms

- Anatomy
- Pharyngeal dilator muscle control asleep
- Arousal Threshold
- Loop gain
- Lung volume
- Vascular

AIRWAY MUSCLE ACTIVITY IN OSA

Airway Dilator Muscle Activity and Lung Volume During Stable Breathing in Obstructive Sleep Apnea

Amy S. Jordan, PhD[1,2]; David P. White, MD[1,2]; Yu-Lun Lo, MD[3]; Andrew Wellman, MD[1,2]; Danny J. Eckert, PhD[1,2]; Susie Yim-Yeh, MD[1,2]; Matthias Eikermann, MD[1,2]; Scott A. Smith[1]; Karen E. Stevenson[1]; Atul Malhotra, MD[1,2]

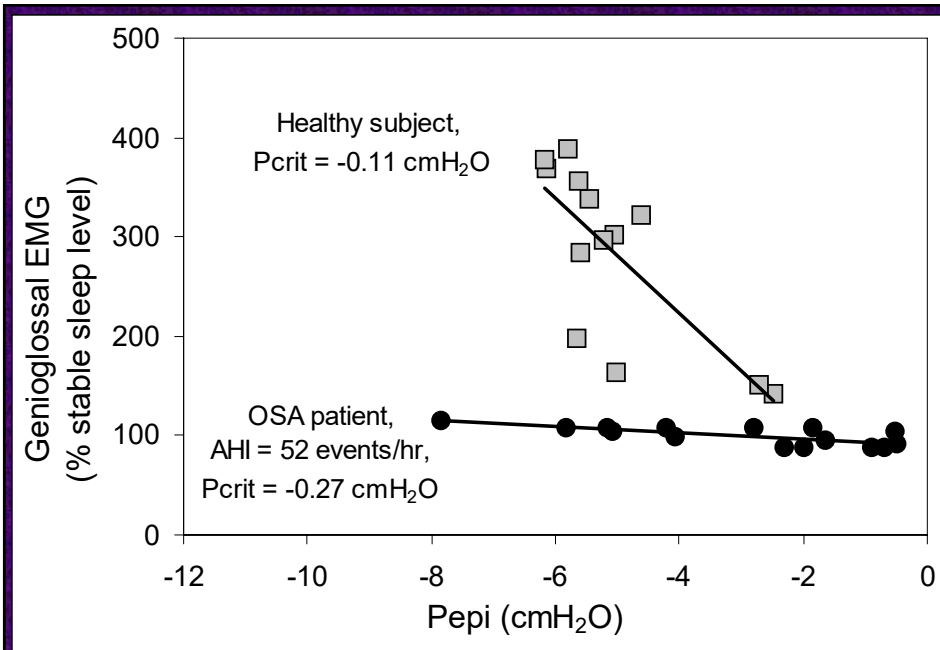
[1]Division of Sleep Medicine, Harvard Medical School, Boston, MA; [2]Sleep Disorders Research Program, Brigham and Women's Hospital, Boston, MA; [3]Department of Thoracic Medicine, Chang Gang Memorial Hospital, Taipei, Taiwan

Most OSA patients have some periods of stable breathing

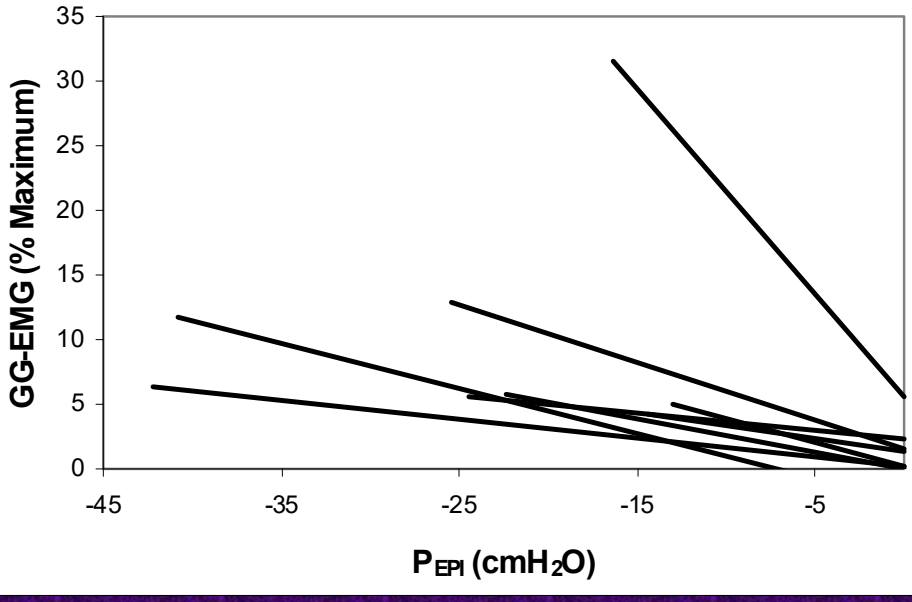
- Studied GGEMG, TPEMG, EELV etc
- Genioglossus activity was invariably high during stable breathing

- Concept: Genioglossus is necessary and sufficient to stabilize breathing spontaneously in OSA

Sleep 2009



Sands et al. AJRCCM 2014



Arousal Threshold – Double-edged Sword

- A low arousal threshold could lead to premature arousal with inadequate time to accumulate respiratory stimuli
- A high arousal threshold could lead to substantial hypoxemia and hypercapnia with end-organ impact

- Therapies to manipulate arousal threshold are likely to benefit some patients and theoretically hurt others

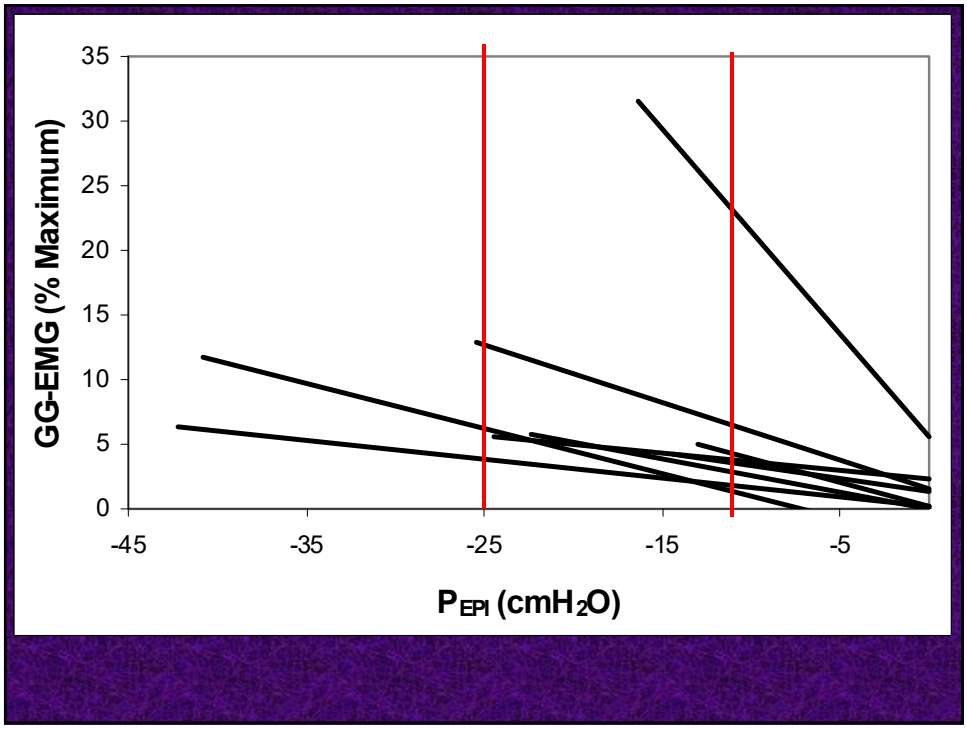
ORIGINAL RESEARCH

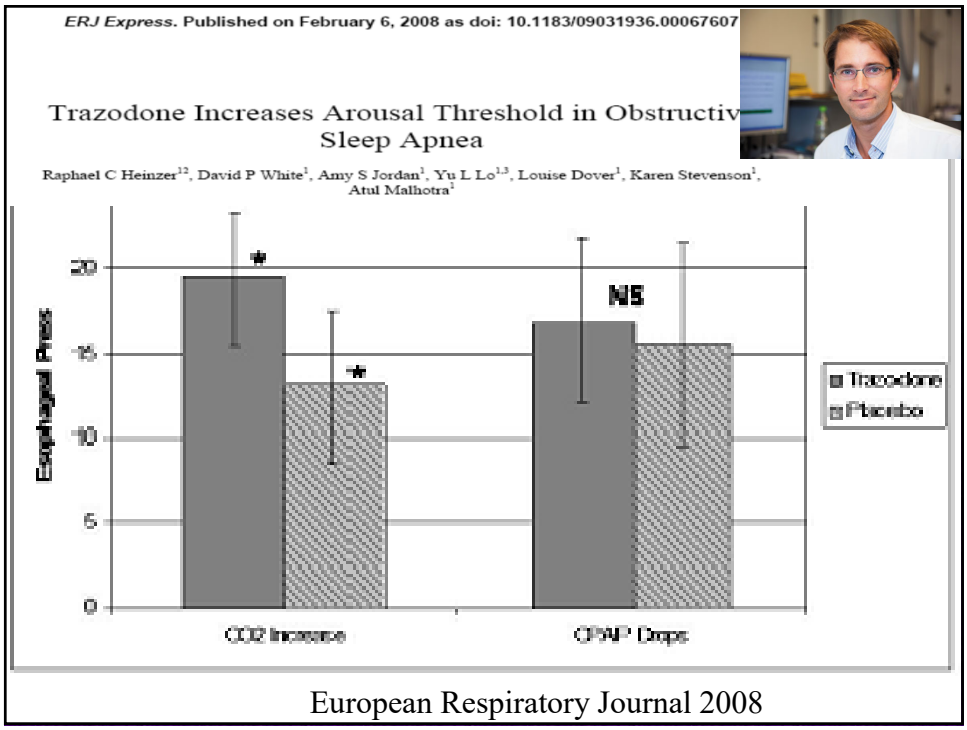
Trazodone Effects on Obstructive Sleep Apnea and Non-REM Arousal Threshold

Erik T. Smales[1,2], Bradley A. Edwards[2], Pam N. Deyoung[1,2], David G. McSharry[2], Andrew Wellman[2], Adrian Velasquez[2,3], Robert Owens[1,2], Jeremy E. Orr[1], and Atul Malhotra[1,2]

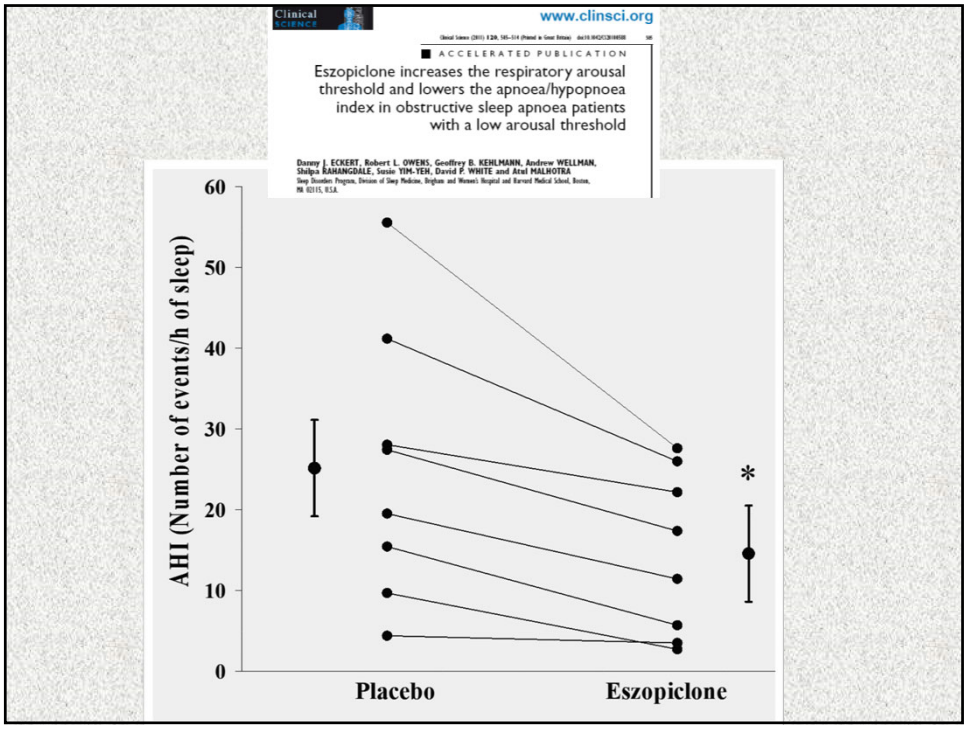
[1]Division of Pulmonary and Critical Care Medicine, University of California San Diego, La Jolla, CA; [2]Division of Sleep Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA; and [3]Dartmouth Hitchcock Medical Center, Lebanon, New Hampshire

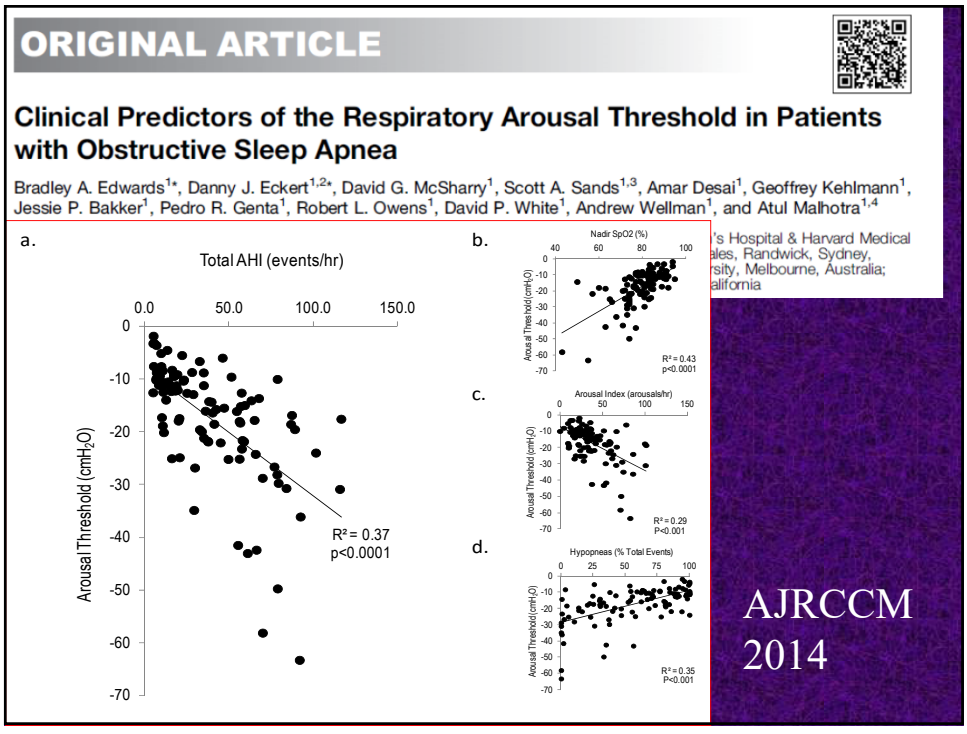
Saboisky et al. Thorax 2010; Smales et al. Annals ATS 2015





European Respiratory Journal 2008


Clinical SCIENCE
www.clinsci.org
ACCELERATED PUBLICATION
Eszopiclone increases the respiratory arousal threshold and lowers the apnoea/hypopnoea index in obstructive sleep apnoea patients with a low arousal threshold
Danny J. ECKERT, Robert L. OWENS, Geoffrey B. KEHLMANN, Andrew WELLMAN, Shilpa RAHANGDALE, Susie YIM-YEH, David P. WHITE and Atul MALHOTRA
AHI (Number of events/h of sleep)
60
50
40
30
20
10
0
*
Placebo
Eszopiclone


ORIGINAL ARTICLE
Clinical Predictors of the Respiratory Arousal Threshold in Patients with Obstructive Sleep Apnea
Bradley A. Edwards[1]*, Danny J. Eckert[1,2]*, David G. McSharry[1], Scott A. Sands[1,3], Amar Desai[1], Geoffrey Kehlmann[1], Jessie P. Bakker[1], Pedro R. Genta[1], Robert L. Owens[1], David P. White[1], Andrew Wellman[1], and Atul Malhotra[1,4]
's Hospital & Harvard Medical
ales, Randwick, Sydney,
rsity, Melbourne, Australia;
alifornia
a.
Total AHI (events/hr)
0.0
50.0
100.0
150.0
0
-10
-20
-30
-40
-50
-60
-70
Arousal Threshold (cmH2O)
R² = 0.37
p<0.0001
b.
Nadir SpO2 (%)
40
60
80
100
Arousal Threshold (cmH2O)
R² = 0.43
p<0.0001
c.
Arousal Index (arousals/hr)
0
50
100
150
Arousal Threshold (cmH2O)
R² = 0.29
P<0.001
d.
Hypopneas (% Total Events)
0
25
50
75
100
Arousal Threshold (cmH2O)
R² = 0.35
P<0.001
AJRCCM
2014

Arousal Threshold

- >60% of variance in arousal threshold is predicted with AHI, nadir saturation and % hypopneas
- Clinical prediction of arousal threshold may help to guide response to sedative/hypnotics

Editorial

Potential protective mechanism of arousal in obstructive sleep apnea

Naomi Deacon, Atul Malhotra

Editorial

The importance of arousal in obstructive sleep apnea—updates from the American Thoracic Society 2016

Atul Malhotra[1], Amy Jordan[2]

Journal Thoracic Disease 2016

Pharyngeal Muscle Control

- There are likely to be subgroups of patients who respond to efforts to augment muscle activation
- Perhaps targeting this subgroup would make sense in pharmacological studies
- Increasing upper airway muscle responsiveness may be <u>deleterious</u> in patients with unstable ventilatory control

PHYSIOLOGY IS MEDICINE

PHYSIOLOGY 29: 153–155, 2014; doi:10.1152/physiol.00013.2014

Atul Malhotra,[1] Naomi Deacon,[2] Frank Powell,[1] and Eliot S. Katz[3]
[1]University of California-San Diego, La Jolla, California; [2]University of Adelaide, Australia; and [3]Harvard Medical School, Boston, Massachussets

Adaptive Responses Using Obstructive Sleep Apnea as the Paradigm

several studies investigating pharmacological strategies, e.g., using sedative/hypnotic agents to increase arousal threshold,

Obstructive Sleep Apnea
Underlying Mechanisms

- Anatomy
- Pharyngeal dilator muscle control asleep
- Arousal Threshold
- Loop gain
- Lung volume

Loop Gain

- **measure of the stability of negative feedback control system**

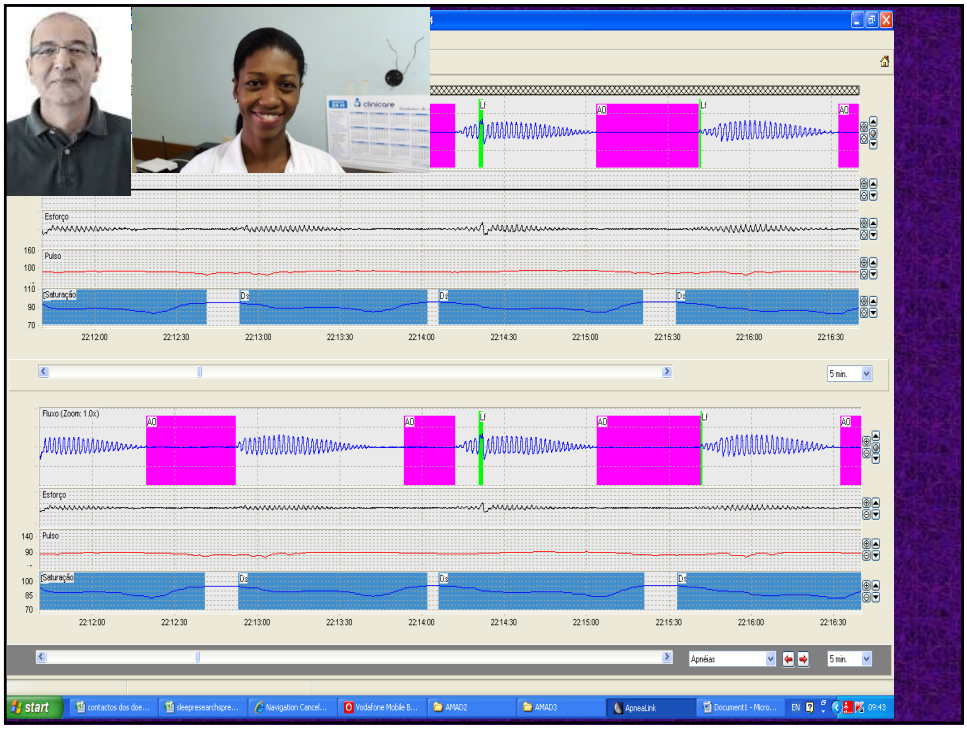
Younes AJRCCM 2001

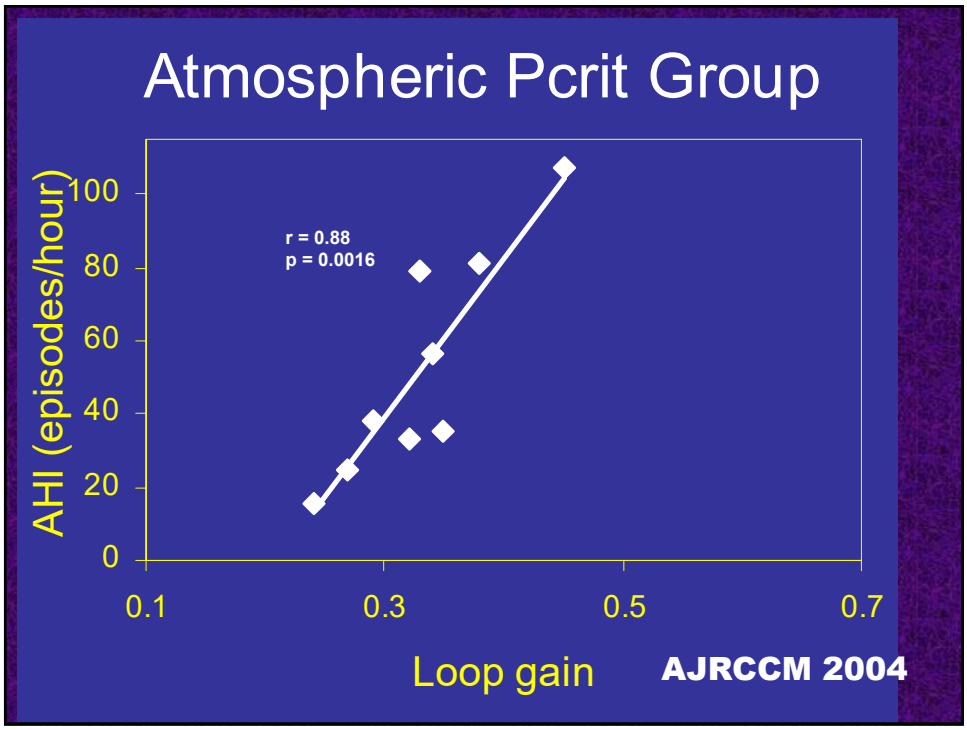
- **Thermostat analogy**

Inherent vs. Induced Loop Gain Abnormalities in Obstructive Sleep Apnea

Naomi Deacon-Diaz and Atul Malhotra*

Deacon and Malhotra Frontiers in Neurology in press; Sleep in press


Esforço
Pulso
Saturação
Fluxo (Zoom: 1.0x)
Apnéias
start


Atmospheric Pcrit Group
AHI (episodes/hour)
100
80
60
40
20
0
r = 0.88
p = 0.0016
0.1
0.3
0.5
0.7
Loop gain
AJRCCM 2004

JCSM
Journal of Clinical Sleep Medicine

SCIENTIFIC INVESTIGATIONS

Physiology-Based Modeling May Predict Surgical Treatment Outcome for Obstructive Sleep Apnea

Yanru Li, MD[1,2]; Jingying Ye, MD[1,3]; Demin Han, MD, PhD[1]; Xin Cao, MD[1]; Xiu Ding[1]; Yuhuan Zhang[1,3]; Wen Xu, MD[1]; Jeremy Orr, MD[2]; Rachel Jen, MD[2]; Scott Sands, PhD[4,5]; Atul Malhotra, MD[2]; Robert Owens, MD[2]

High LG predicts surgical failure
LG lowers after surgery suggesting is partially acquired
Low AT predicts surgical failure ? Therapeutic target

Results: Although preoperative loop gain was positively correlated with postoperative apnea-hypopnea index (AHI) ($P = .008$) and arousal threshold was negatively correlated ($P = .011$), in both model 1 and 2, the only significant variable was preoperative AHI, which explained 42% of the variance in postoperative AHI. In contrast, the physiological model (model 3), which included AHI_{REM} (anatomy term), fraction of events that were hypopnea (arousal term), the ratio of AHI_{REM} and AHI_{NREM} (muscle responsiveness term), loop gain, and central/mixed apnea index (control of breathing terms), was able to explain 61% of the variance in postoperative AHI.

Conclusions: Although loop gain and arousal threshold are associated with residual AHI after surgery, only preoperative AHI was predictive using multivariate regression modeling. Instead, incorporating selected surrogates of physiological traits on the basis of OSA pathophysiology created a model that has more association with actual residual AHI.

JCSM 2017

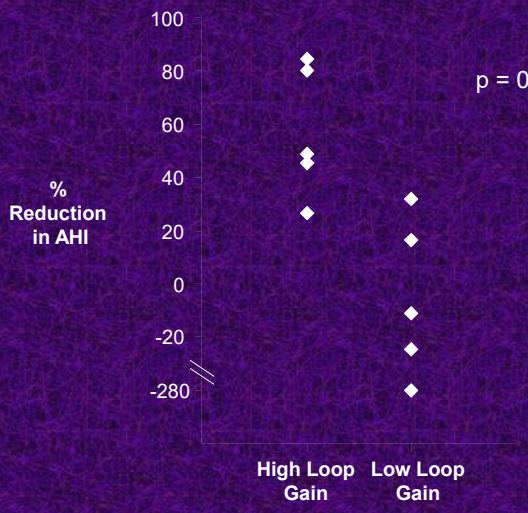
Obstructive Sleep Apnea
Underlying Mechanisms
High Loop Gain

Administer agents to reduce loop gain:

- **Oxygen** (Resp Phys 2008, ERJ 2018)
- **Acetazolamide** (Sleep 2013, J. Physiol. 2012, ATS 2019)

- **Loop gain can be manipulated pharmacologically in a subset of OSA**

Effect of Oxygen Between Groups



Resp Physiol 2008

ERJ 2018

Obstructive Sleep Apnea
Potential Therapies

- Oropharyngeal exercise
- Hypoglossal nerve stimulation
- Winx
- Provent
- Postural therapy
- Bariatric surgery

Effects of Oropharyngeal Exercises on Patients with Moderate Obstructive Sleep Apnea Syndrome

Kátia C. Guimarães[1], Luciano F. Drager[1], Pedro R. Genta[1], Bianca F. Marcondes[1], and Geraldo Lorenzi-Filho[1]

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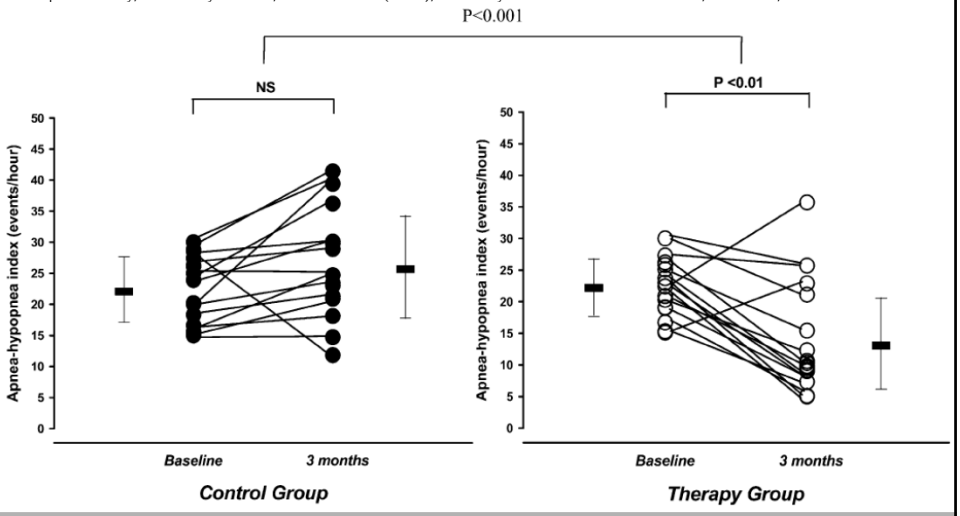

AJRCCM 2009

CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of MEDICINE®

Exercise Is Associated with a Reduced Incidence of Sleep-disordered Breathing

Karim M. Awad, MD,[a] Atul Malhotra,[a] Jodi H. Barnet,[b] Stuart F. Quan,[a,c] Paul E. Peppard[b]

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Table 2 Association of Exercise and Incidence of Mild and Moderate SDB*

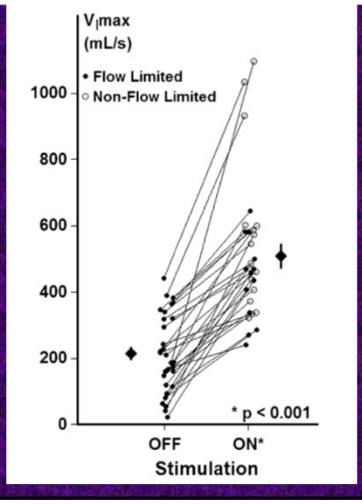
		Adjusted†	
	n	Odds Ratio (95% CI)	*P* Value
Incidence of AHI ≥5/h§			
Baseline exercise (trend)‖	763	0.76 (0.62-0.94)	.011
Baseline exercise (≥4h/week vs no exercise)	763	0.59 (0.39-0.89)	.012
Incidence of AHI ≥15/h§			
Baseline exercise (trend)‖	959	0.67 (0.51-0.87)	.002
>Baseline exercise (≥4 h/week vs no exercise)	959	0.47 (0.28-0.79)	.004

AJM 2012

Acute Upper Airway Responses to Hypoglossal Nerve Stimulation during Sleep in Obstructive Sleep Apnea

Alan R. Schwartz[1], Maree Barnes[2], David Hillman[3], Atul Malhotra[4], Eric Kezirian[5], Philip L. Smith[1], Thomas Hoegh[6], Daniel Parrish[6], and Peter R. Eastwood[3,7]

[1]Johns Hopkins School of Medicine, Baltimore, Maryland; [2]Austin Hospital, Melbourne, Australia; [3]Sir Charles Gairdner Hospital, Perth, Australia; [4]Brigham and Womens Hospital, Boston, Massachusetts; [5]University of California at San Francisco, San Francisco, California; [6]Apnex Medical, St. Paul, Minnesota; and [7]Centre for Sleep Science, School of Anatomy and Human Biology, University of Western Australia, Perth, Australia



AJRCCM 2012

Acute Upper Airway Responses to Hypoglossal Nerve Stimulation during Sleep in Obstructive Sleep Apnea

Alan R. Schwartz[1], Maree Barnes[2], David Hillman[3], Atul Malhotra[4], Eric Kezirian[5], Philip L. Smith[1], Thomas Hoegh[6], Daniel Parrish[6], and Peter R. Eastwood[3,7]

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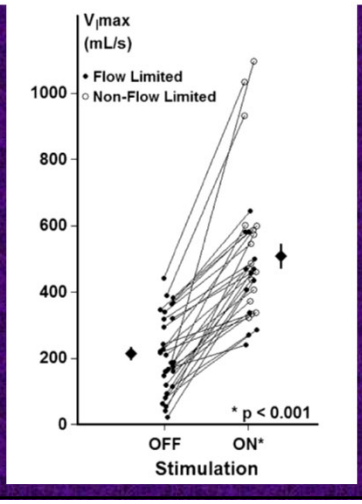


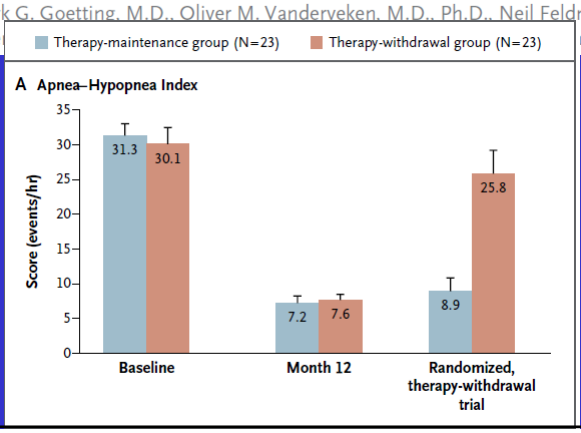
Speculation: progressive reductions in airflow may reflect UA muscle dysfunction which could be amenable to hypoglossal nerve stimulation or pharmacotherapy

AJRCCM 2012

ORIGINAL ARTICLE

Upper-Airway Stimulation for Obstructive Sleep Apnea

Patrick J. Strollo, Jr., M.D., Ryan J. Soose, M.D., Joachim T. Maurer, M.D., Nico de Vries, M.D., Jason Cornelius, M.D., Oleg Froymovich, M.D., Ronald D. Hanson, M.D., Tapan A. Padhya, M.D., David L. Steward, M.D., M. Boyd Gillespie, M.D., B. Tucker Woodson, M.D., Paul H. Van de Heyning, M.D., Ph.D., Mark G. Goetting, M.D., Oliver M. Vanderveken, M.D., Ph.D., Neil Feldman, M.D., Le… …l Group*



NEJM 2014; OHNS 2018

The NEW ENGLAND JOURNAL of MEDICINE

Hypoglossal-Nerve Stimulation for Obstructive Sleep Apnea

Atul Malhotra, M.D.

- NEJM 2014 Strollo et al. showed potential benefit to HGNS for OSA
- Unclear which patients might respond best
- Underlying mechanism of OSA is likely to be important predictor

Stimulating therapy for obstructive sleep apnoea

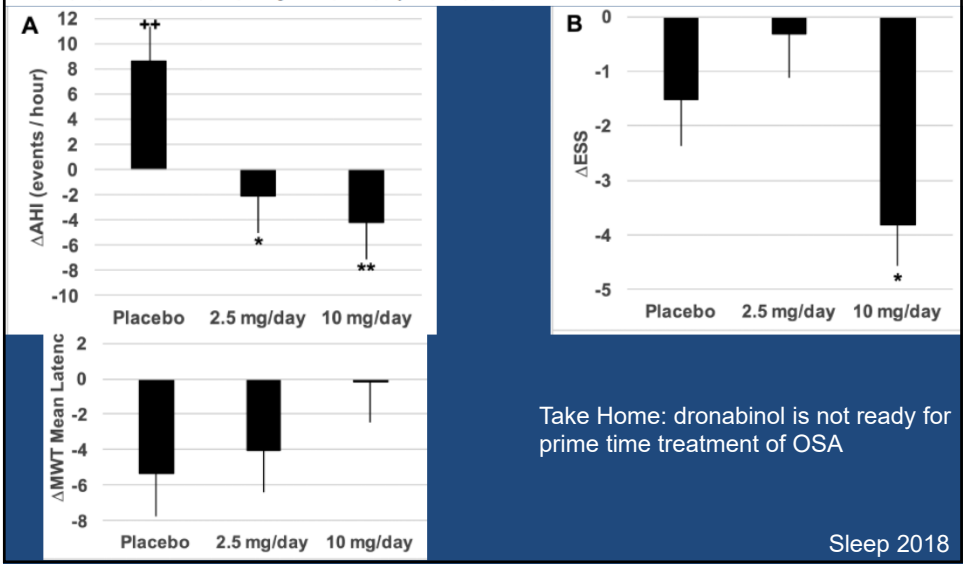
Patrick J Strollo Jr,[1] Atul Malhotra[2]

NEJM 2014; Thorax 2016

ORIGINAL ARTICLE

Pharmacotherapy of Apnea by Cannabimimetic Enhancement, the *PACE* Clinical Trial: Effects of Dronabinol in Obstructive Sleep Apnea

David W. Carley, PhD[1,2,3], Bharati Prasad, MD[2,3,4], Kathryn J. Reid, PhD[5,6], Roneil Malkani, MD[5,6], Hryar Attarian, MD[5,6], Sabra M. Abbott, MD, PhD[5,6], Boris Vern, MD, PhD[1,3,†], Hui Xie, PhD[7], Chengbo Yuan, MPH[7], Phyllis C. Zee, MD, PhD[5,6]

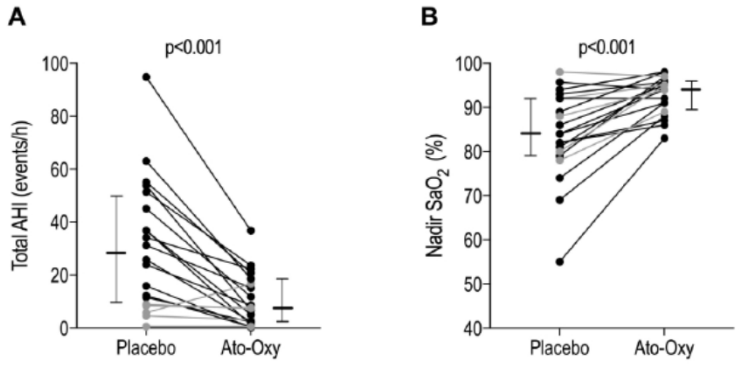


Take Home: dronabinol is not ready for prime time treatment of OSA

Sleep 2018

The Combination of Atomoxetine and Oxybutynin Greatly Reduces Obstructive Sleep Apnea Severity: A Randomized, Placebo-Controlled, Double-Blind Crossover Trial

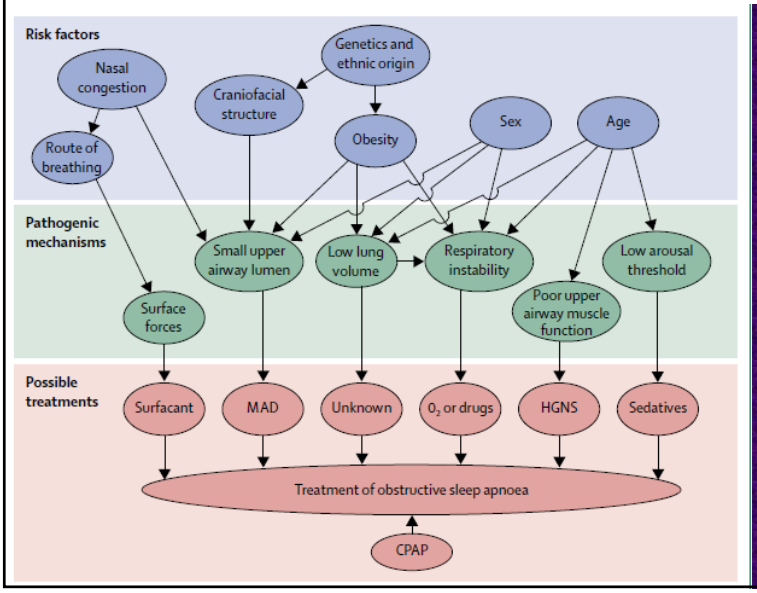
Luigi Taranto-Montemurro[1], Ludovico Messineo[1,2], Scott A Sands[1], Ali Azarbarzin[1], Melania Marques[1,3], Bradley A Edwards[4,5], Danny J Eckert[6], David P White[1] and Andrew Wellman[1].



AJRCCM in press; small numbers, one night only

Adult obstructive sleep apnoea

Amy S Jordan, David G McSharry, Atul Malhotra



Lancet 2014

Vision - Summary

To be able to assess an individual at risk of OSA using a blood test and/or simplified home recording or wearable technology to make diagnosis and WHY

To use this information to determine optimal therapy by assessing responsiveness to interventions and risk of particular complications.

To use real-time patient feedback technologies to optimize adherence and to guide interventions.

Exosomal Cargo Properties, Endothelial Function and Treatment of Obesity Hypoventilation Syndrome Bhattacharjee et al. JCSM 2018

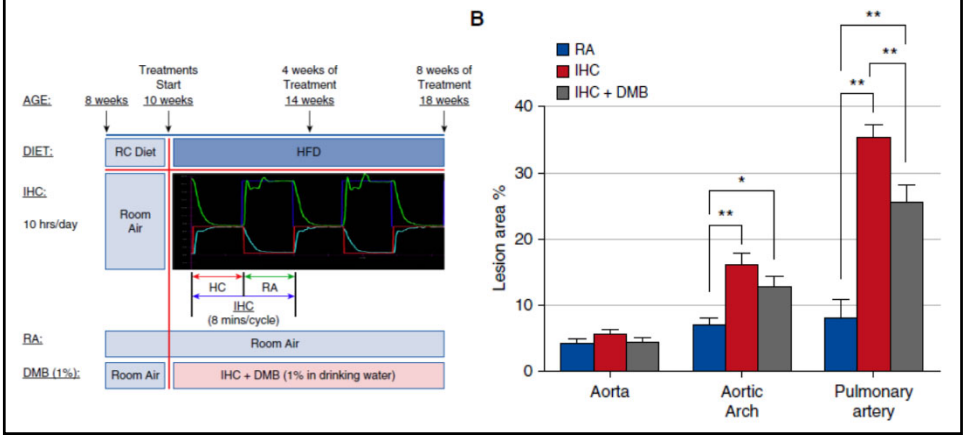
-Can isolate extracellular vesicles and miRNA from human plasma from untreated OSA
-take the exosomes and introduce into mice or cell culture systems
-assess impact on endothelial cells including monocyte adhesion, eNOS, tight junctions
-can take exosomes after CPAP treatment of OSA and reassess
-provide direct evidence of vascular benefit of CPAP

ORIGINAL RESEARCH AJRCMB 2017

Intermittent Hypoxia and Hypercapnia Accelerate Atherosclerosis, Partially via Trimethylamine-Oxide

Jin Xue[1], Dan Zhou[1], Orit Poulsen[1], Toshihiro Imamura[1], Yu-Hsin Hsiao[1], Travis H. Smith[1], Atul Malhotra[2], Pieter Dorrestein[1,3,4], Rob Knight[1,4,5], and Gabriel G. Haddad[1,3,5,6]

Departments of [1]Pediatrics, [2]Internal Medicine, and [3]Neurosciences, School of Medicine, [4]School of Pharmacy and Pharmaceutical Sciences, and [5]Department of Computer Sciences and Engineering, School of Engineering, University of California San Diego, La Jolla, California; and [6]The Rady Children's Hospital, San Diego, California



Take Home Points

1. CPAP is treatment of choice for OSA and a defeatist attitude about CPAP is not justifiable
2. Alternative therapies are available which provide acceptable results for select patients
3. Individualized therapy may be viable in the future based on mechanism underlying OSA
4. Exciting time for sleep field