

BSS International Sleep Medicine Course 2026

15th - 18th September | Newcastle

Sleep-related breathing disorders - pathophysiology

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British Sleep Society



UK Multidisciplinary Sleep Professionals



Nederlandse vereniging voor
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1. I do not have any potential conflicts to disclose.

☒

2. I wish to disclose the following potential conflicts of interest:

Type of Potential Conflict	Details of Potential Conflict
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Consultant	Aurobindo, Azelis, Bioprojet, Procter & Gamble, SDWorx, TotalCare, Westfalen Medical, ZOLL.
Speakers' Bureaus	
Financial support	
Other	

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3. The material presented in this lecture has no relationship with any of these potential conflicts, **OR**

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4. This talk presents material that is related to one or more of these potential conflicts, and the following objective references are provided as support for this lecture:

- 1.
- 2.
- 3.

DEFINITION “Obstructive sleep apnoea syndrome”

- ≥ 5 obstructive apnoeas-hypopnoeas /hour of sleep

Plus one or more of the following:

- Complaints of sleepiness
- Non-restorative sleep
- Fatigue
- Insomnia complaints
- Awakening with dyspnoea
- Asphyxia
- Frequently snoring
- Apnoeas witnessed by partner

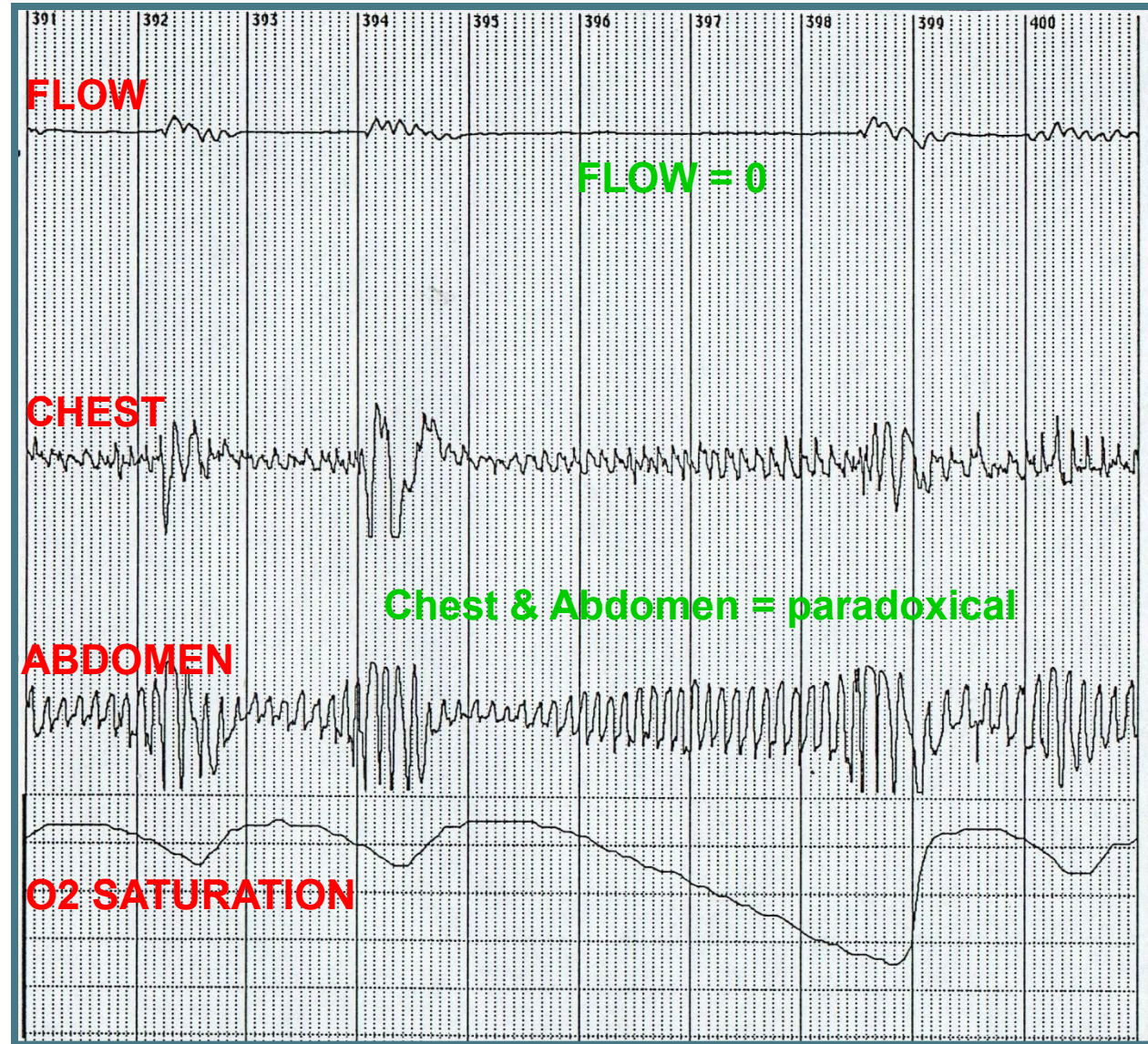
- Diagnosis of : hypertension, mood disturbance, cognitive dysfunction, coronary artery disease, stroke, chronic heart failure, atrial fibrillation, type 2 diabetes

OR

- ≥ 15 obstructive apnoeas-hypopnoeas/ hour of sleep

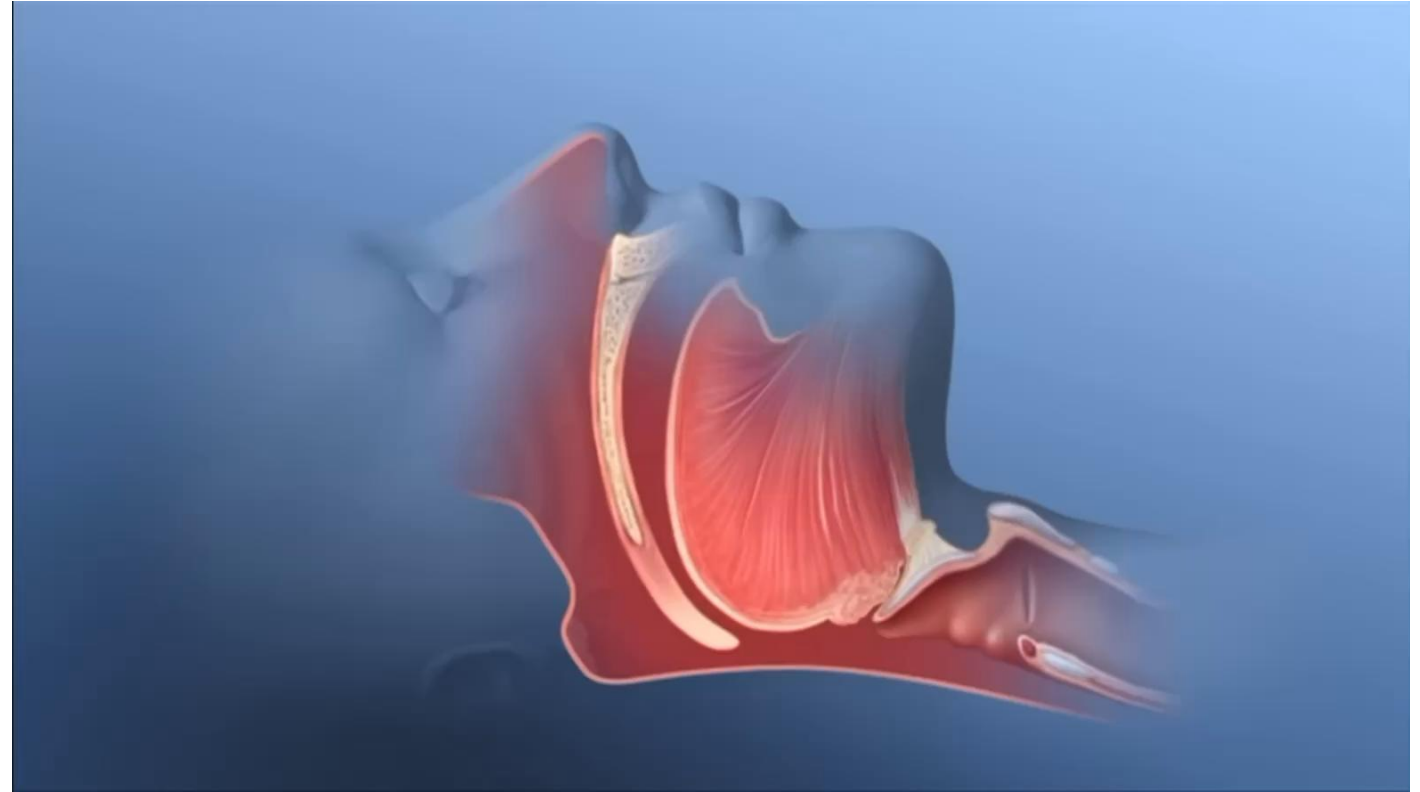
ICSD-3

Repetitive obstructive apnoeas



Obstructive sleep apnoea (OSA)

- Repeated airway collapse → oxygen drop → arousals
- Fragmented sleep, reduced restorative stages
- Results: daytime sleepiness, fatigue, irritability





Pathophysiology OSA

Upper airway collapse may occur due to:

- 1) ↓ UA Size
- 2) Balance of forces
- 3) Increased collapsibility

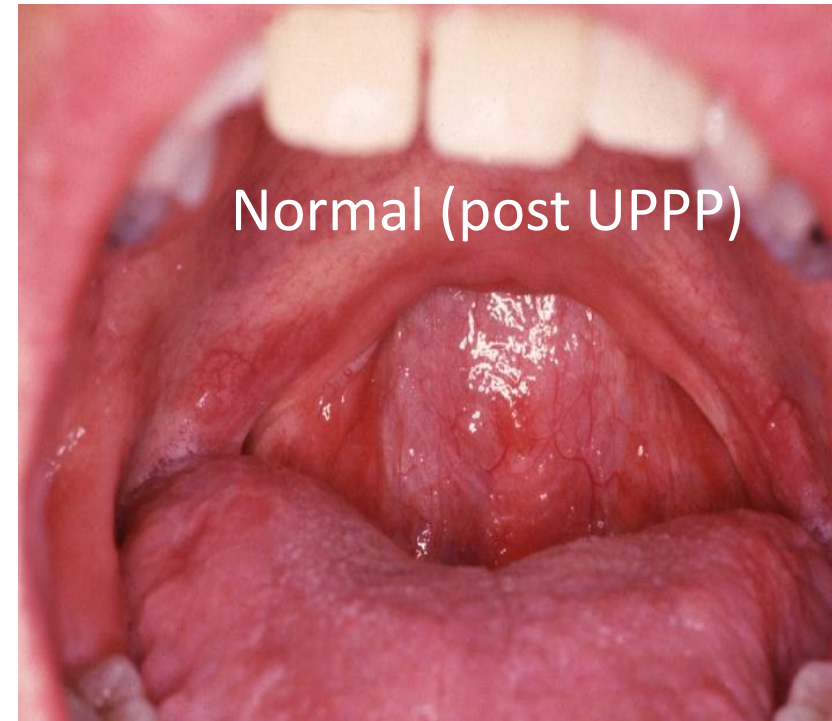
Anatomic abnormality

Imbalance between activation of diaphragm and UA muscles
Impaired reflex activation of UA dilator muscle activity

Airway as a rigid tube with flexible segment

Pathogenesis OSA

↓ UA size: structural abnormalities

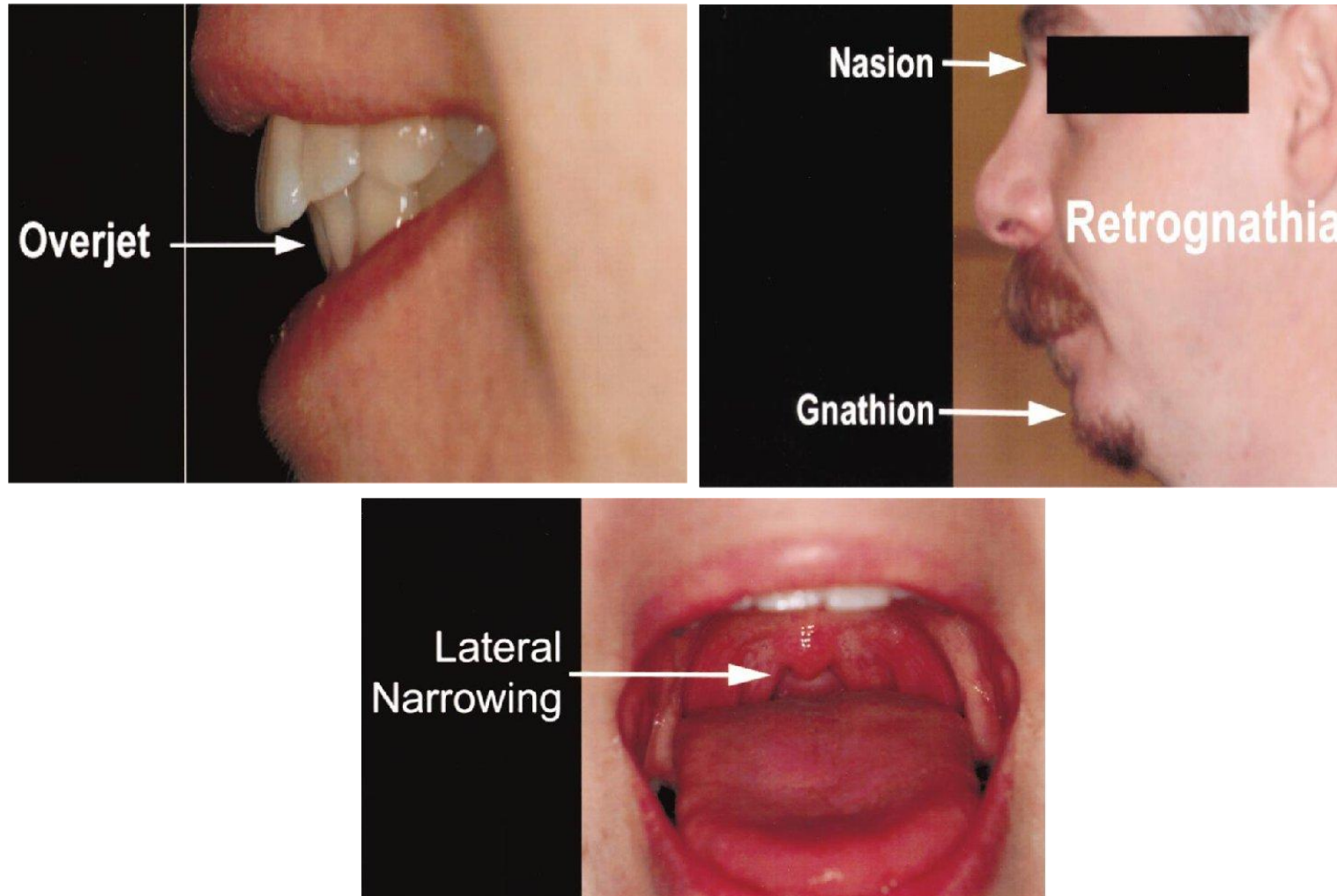


Schellenberg JB et al AJRCCM 2000; 162: 740-8

Pathogenesis OSA

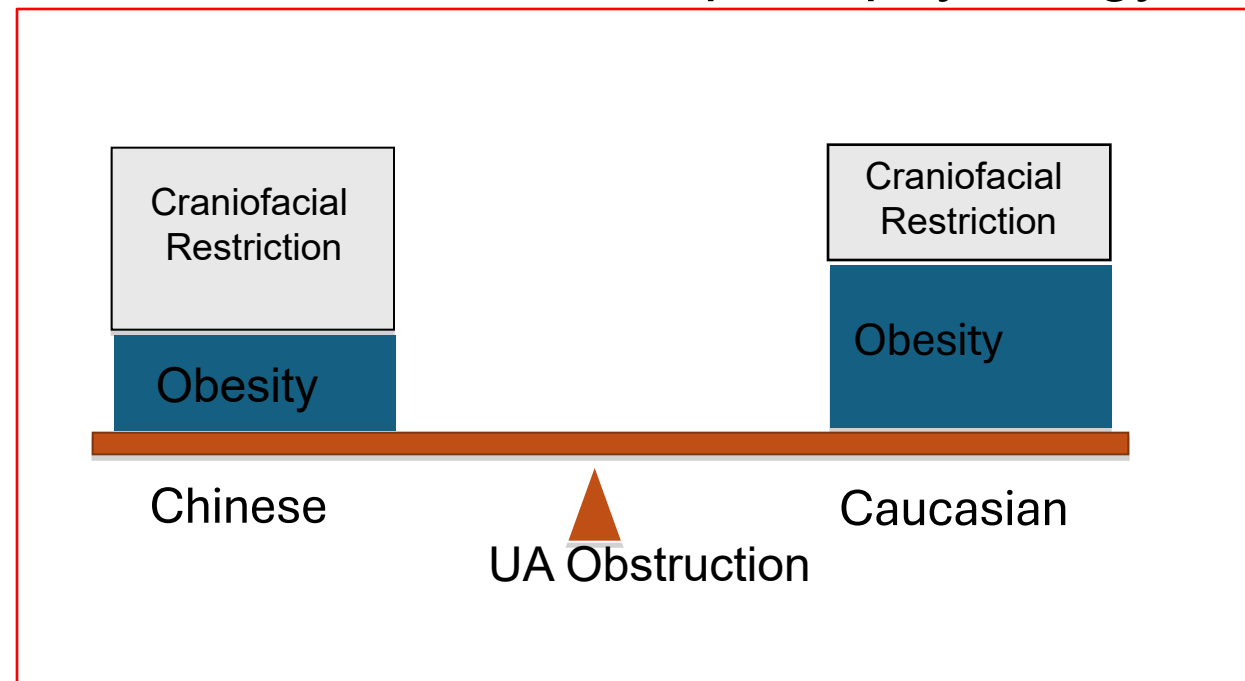
↓ UA size: structural abnormalities

Schellenberg JB et al AJRCCM 2000; 162: 740-8



Influence of ethnicity

Ethnic differences in pathophysiology



Pathogenesis OSA

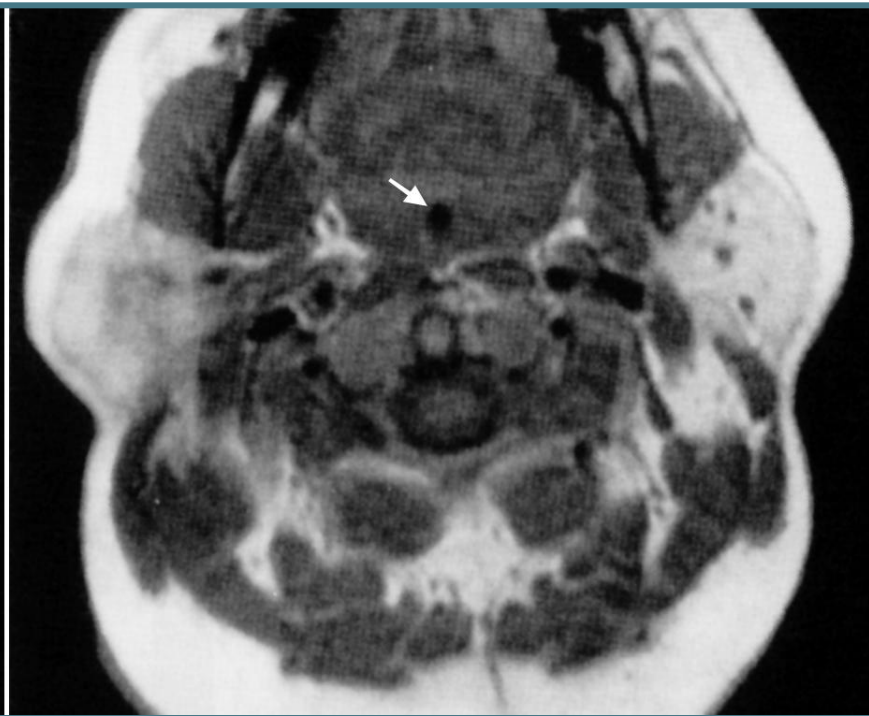
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↓ UA size: structural abnormalities: MRI findings

Normal MRI
(elliptic shape)



Patient MRI
(palatal area)
(circular shape, reduced lateral dimensions)



Schwab et al Am J Respir Crit Care Med 1995;152:1673

Pathogenesis of OSA

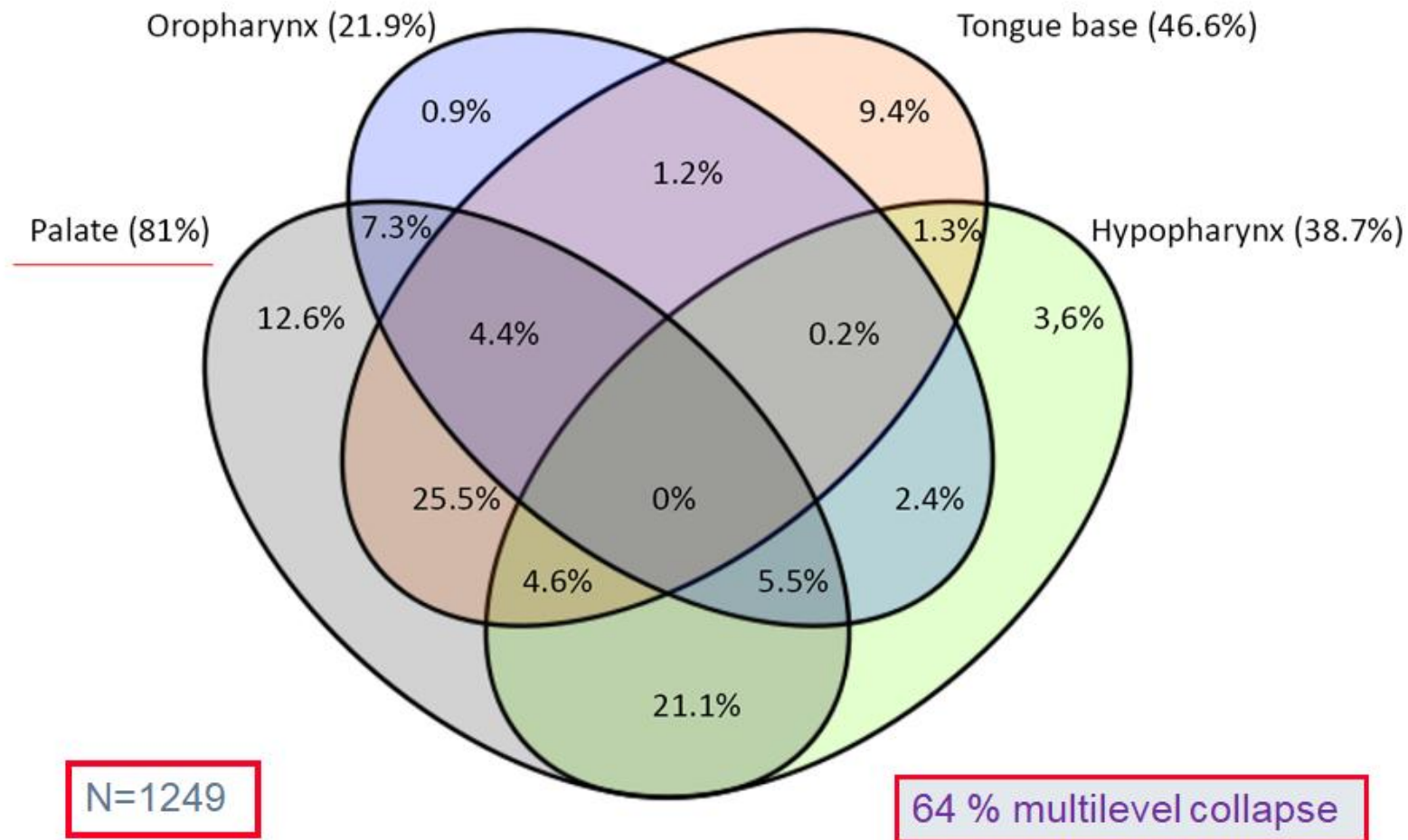
↓ UA size: structural abnormalities

Cephalometric variables and BMI only explain 33% of the variance of AHI

Zucconi et al Thorax 1992;47:157-161

Hypotonic pharynx of sleeping apnoeic patients commonly collapses at multiple sites

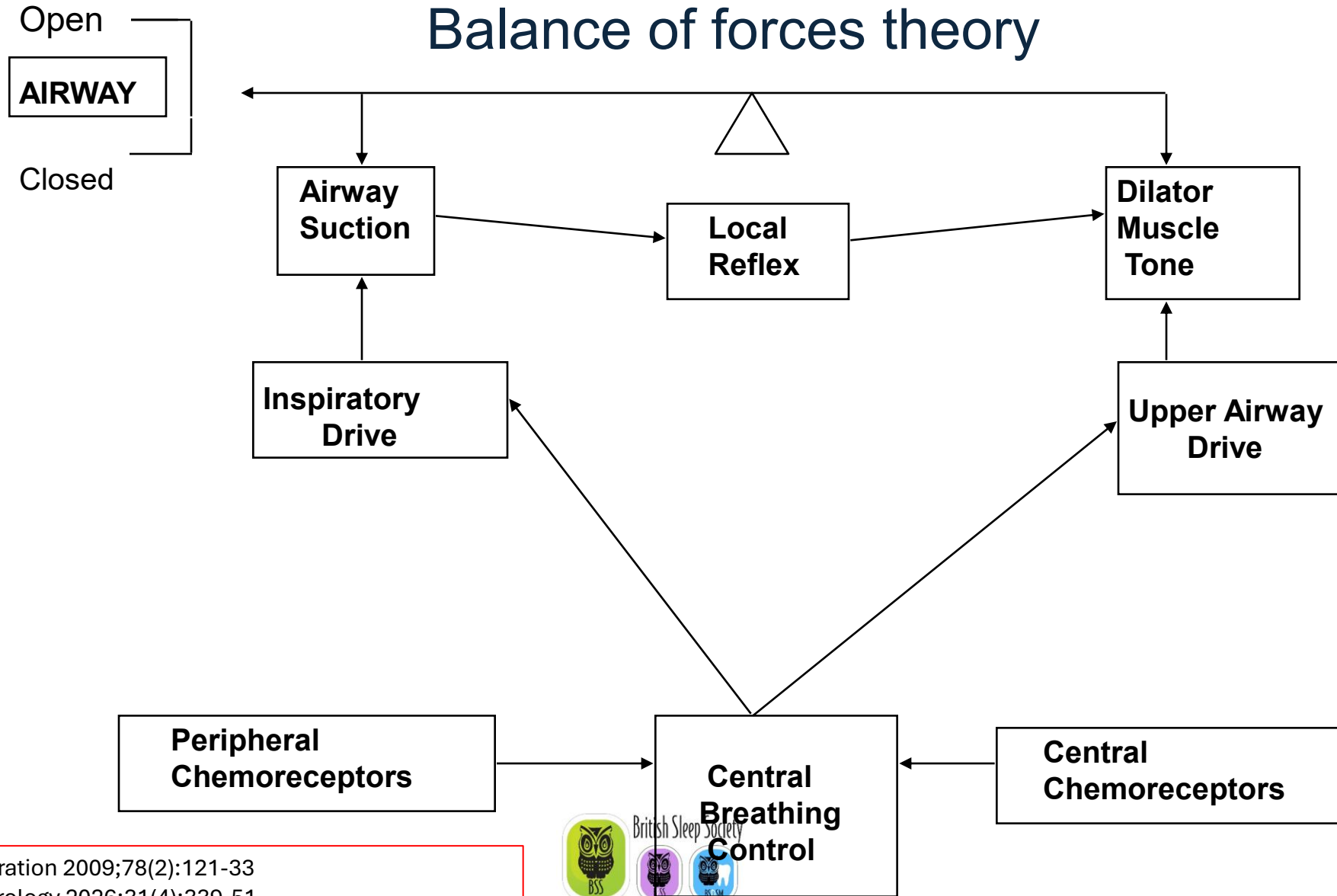
Morrison et al Am Rev Respir Dis 1993;148:606



UZA

Pathogenesis of OSA

Balance of forces theory



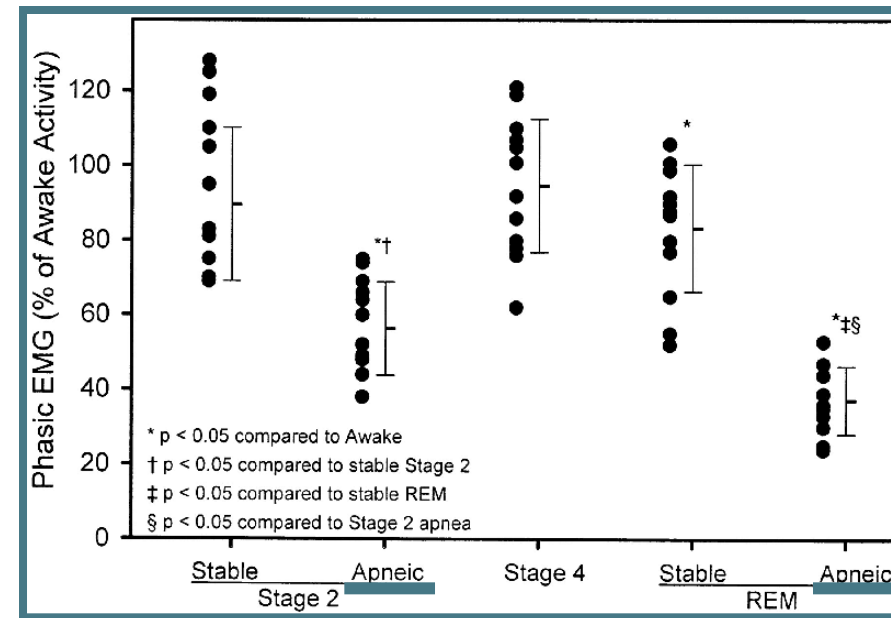
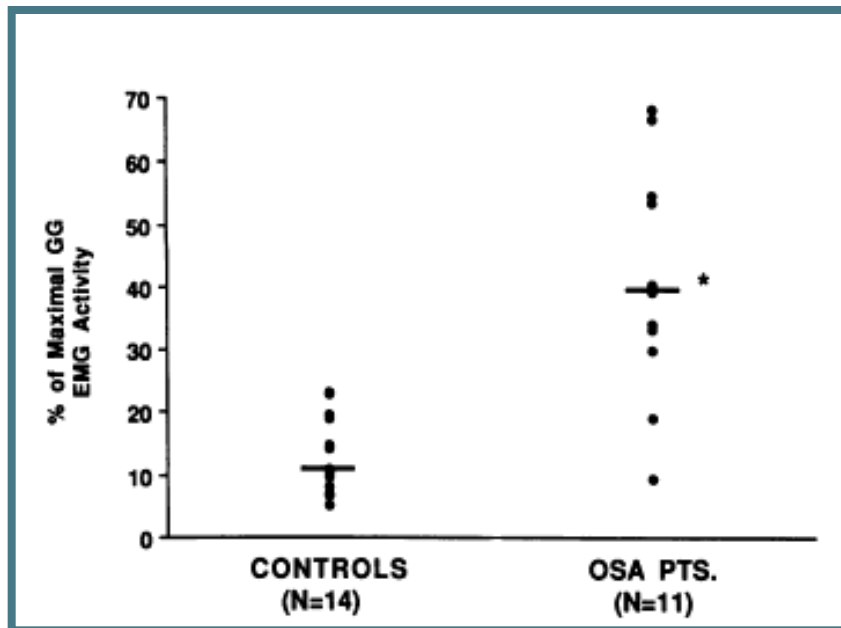
Verbraecken JA et al. Respiration 2009;78(2):121-33
McNicholas WT et al Respirology 2026;31(4):339-51

“Balance of forces”

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M. genioglossus activity in OSA
Disturbed reflex response

- Increased muscle activity in OSA.
- Compensatory mechanism during sleep and wake.
- But: ineffective fascic activity during apnoeas.



Mezzanotte WS et al J Clin Invest 1992; 89: 1571-79
Remmers JE et al J Appl Physiol 1978; 44: 931-8
Katz ES et al AJRCCM 2004; 170: 553-60

“Balance of forces” theory

Impaired reflex response
can be explained by:

- **Nerve lesions**
 - Svanborg 1998, 2001
- **Impairment in sensitivity**
 - Kimoff, 2001
- **Association between *neurological diseases* and OSA**
 - Demattéis, 2001
- **Cellular Inflammation at the UA level**
 - Could be related to the vibrations and trauma of snoring
 - Could alter the functioning of the pharyngeal reflex
 - Paulsen FP et al Am J Respir Crit Care Med 2002;166:501-9
 - Boyd JH et al Am J Respir Crit Care Med 2004;170:541-6
 - Puig F et al Sleep 2005; 28: 1312-6

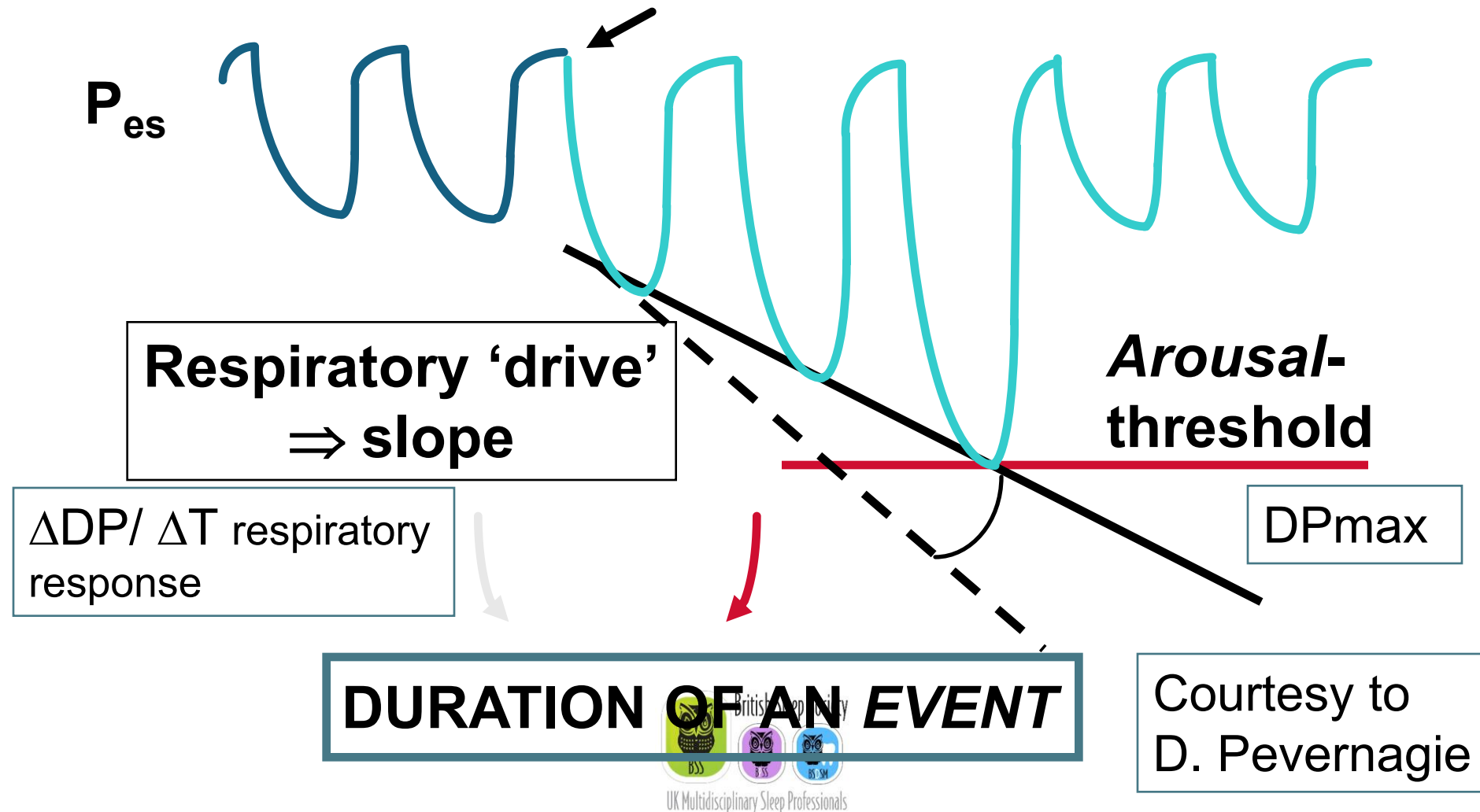
“Balance of forces” theory

Altered chemo-sensitivity

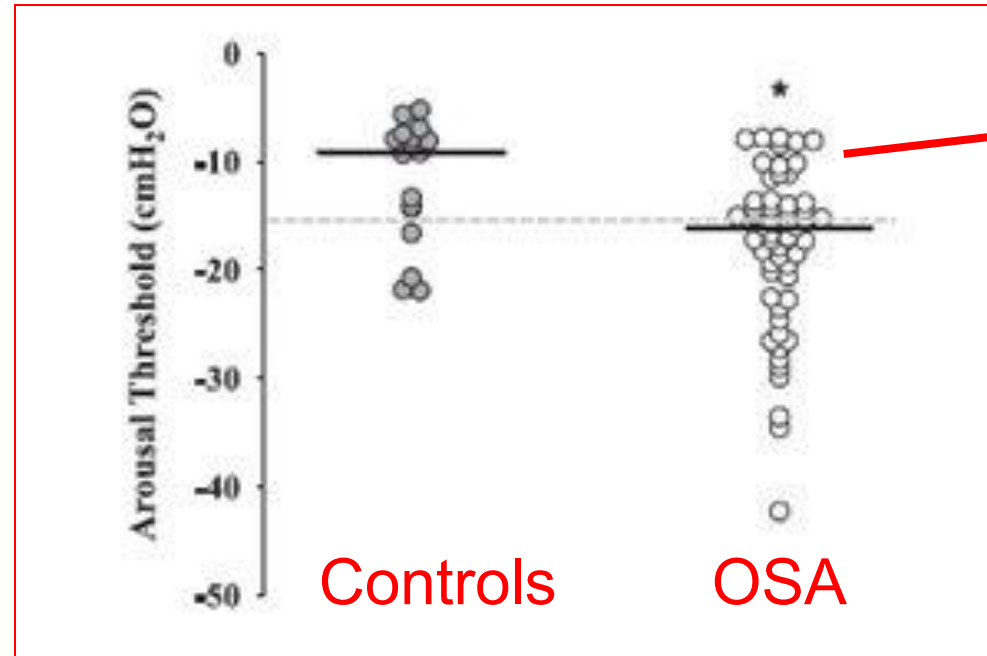
	SHCVR l/min/mmHg	IHCVR mmHg
Controls (n=14)	1.66±0.16	39±1
Heavy snorers (n=14)	1.26±0.20	33±5
Normocapnic OSA (n=14)	2.41±0.26 *	40±2
Hypercapnic OSA (n=11)	0.93±0.23 *	34±6
Overlap OSA (n=11)	2.93±0.38 *	41±2
*p < 0.05 compared to controls		

Verbraecken J et al Respir Physiol 1995;279-87

Response on increased upper airway resistance:
Increased drive and reaching arousal threshold



Arousal threshold



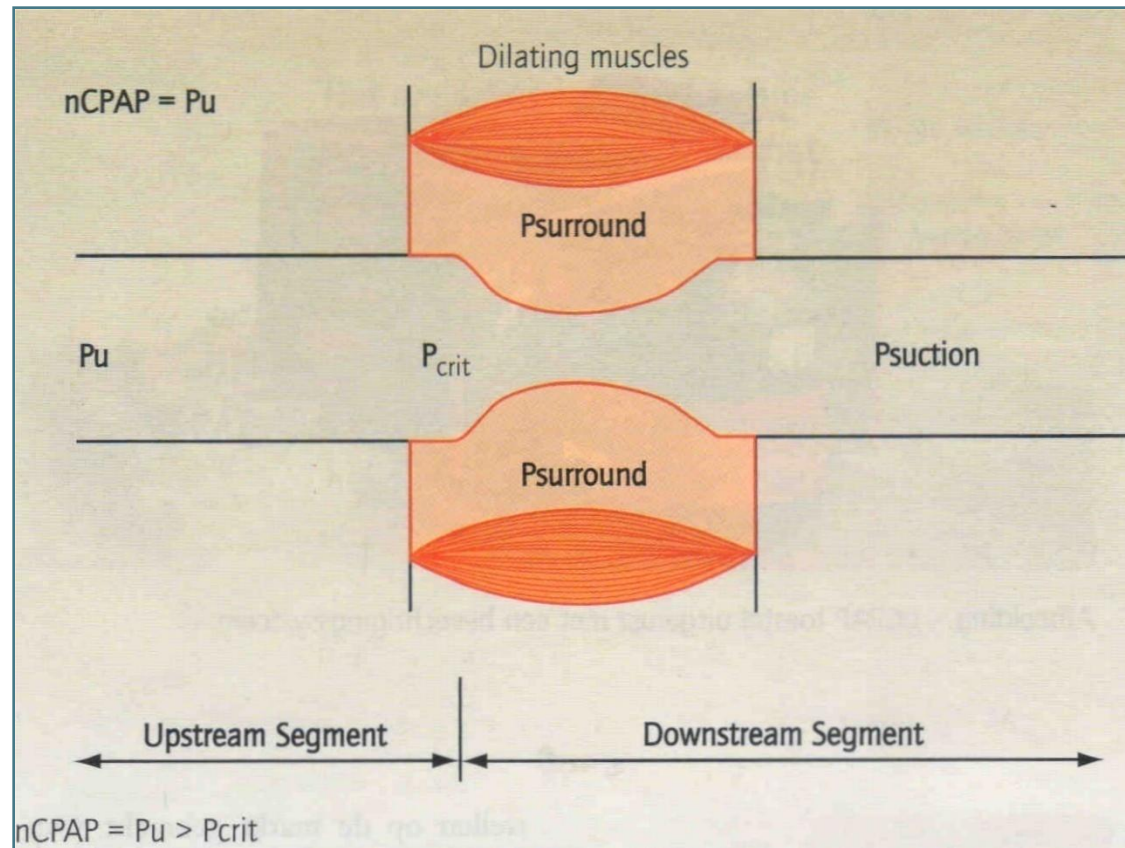
1/3 had
a low
arousal
threshold

Eckert D et al AJRCCM 2013;188(8):996-1004

Pathogenesis OSA

Collapsibility of upper airway

$$V_{\max} = (P_{\text{us}} - P_{\text{crit}}) / R_{\text{us}}$$



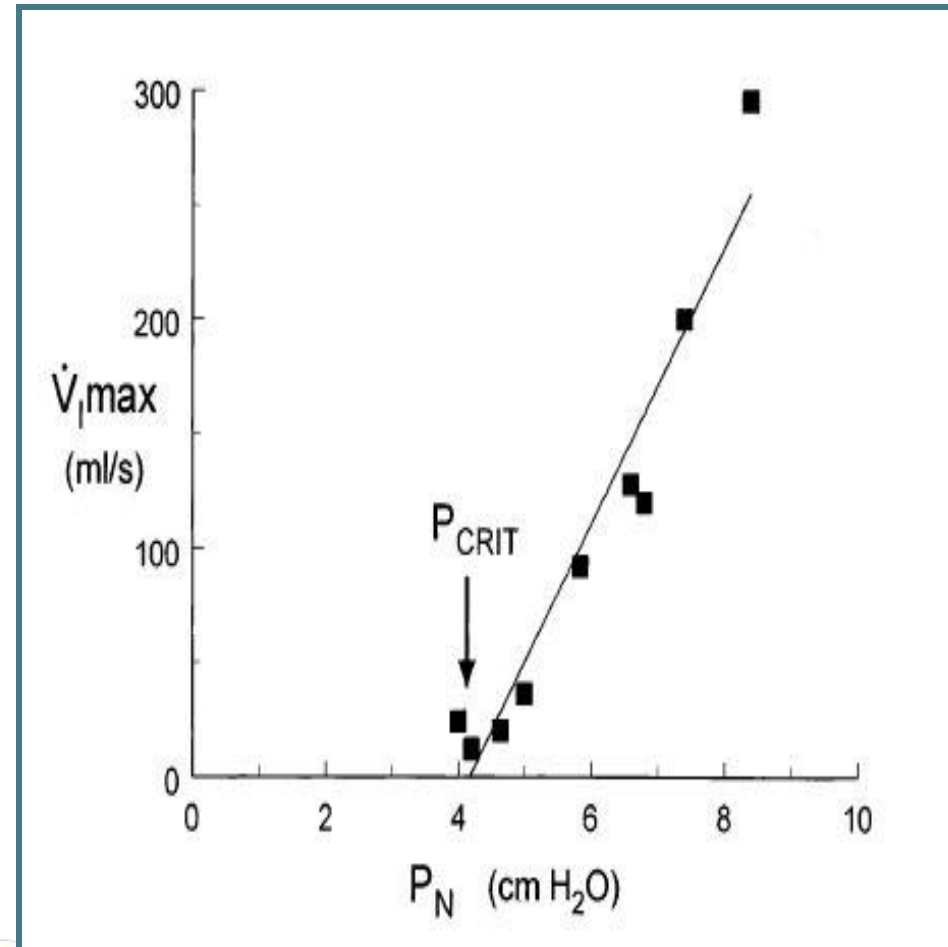
Pathogenesis OSA

Measurement Pcrit: CPAP drop

- During CPAP application
- Protocol:
 - Gradual decrease of CPAP pressure
 - Flow
 - regression/ extrapolation

Schwartz AR et al AJRCCM 1998; 157:1051-7

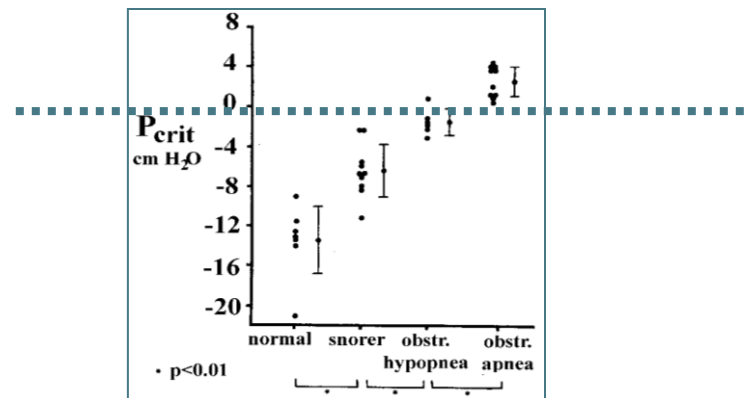
Sforza E et al AJRCCM 1999; 159:149-57



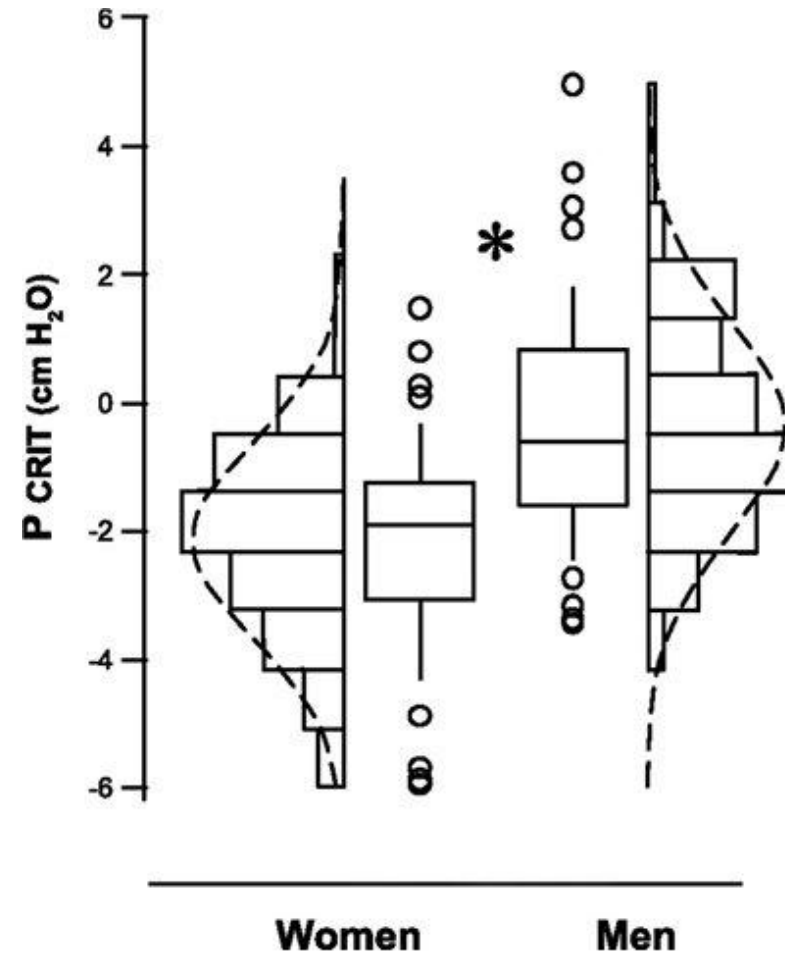
Pathogenesis OSA

Collapsibility of upper airway (3)

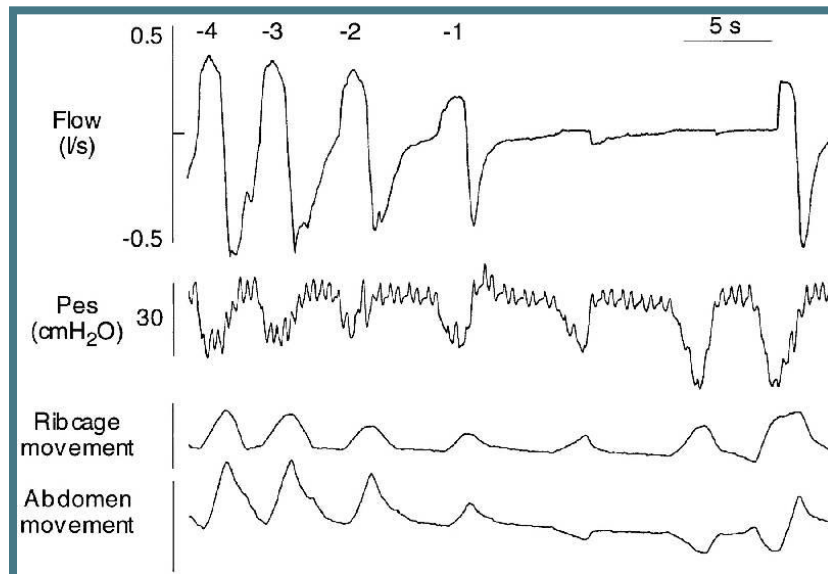
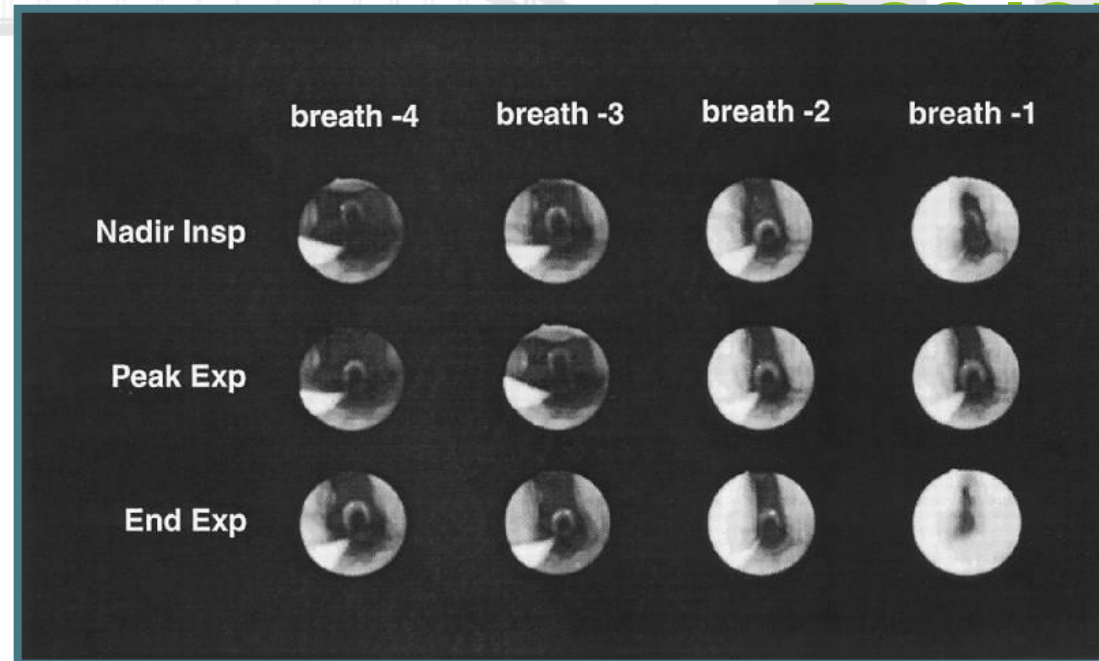
- Normal human upper airway is characterised by a negative Pcrit
 - *Schwartz A et al J Appl Physiol 1988;64:535-42*
- Pcrit correlates with clinical picture of SRBD
 - Pcrit Normals < snorers < OH < OA
 - *Gleadhill et al Am Rev Respir Dis 1991;143:1300-3*



Pcrit higher in men



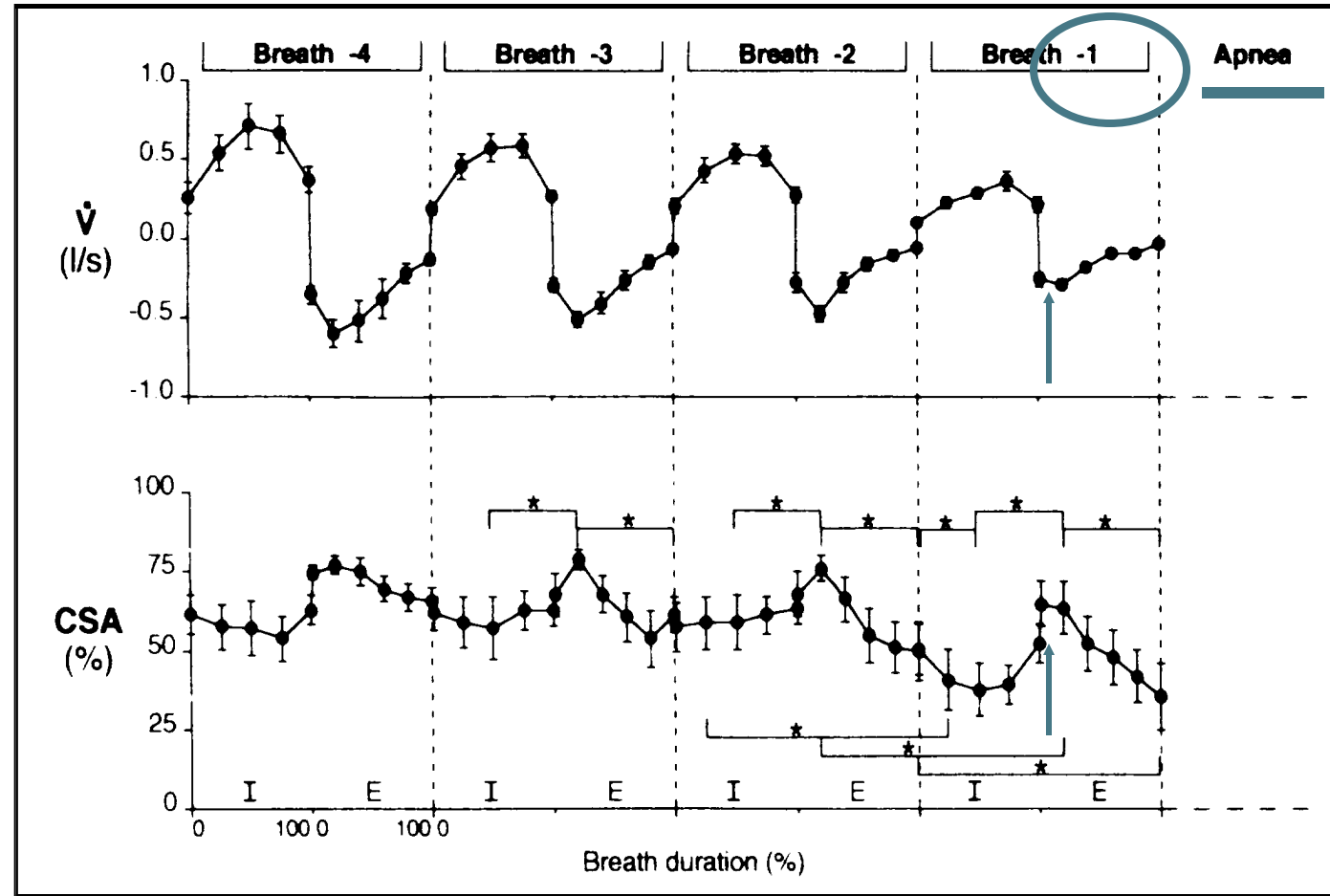
Time course UA collapse: inspiratory or expiratory ?



- 8 OSA patients.
- Fiberoptic imaging.
- Pharyngeal caliber.
- Airflow.
- Oesophageal pressure.
- 4 consecutive breaths preceding occlusion.

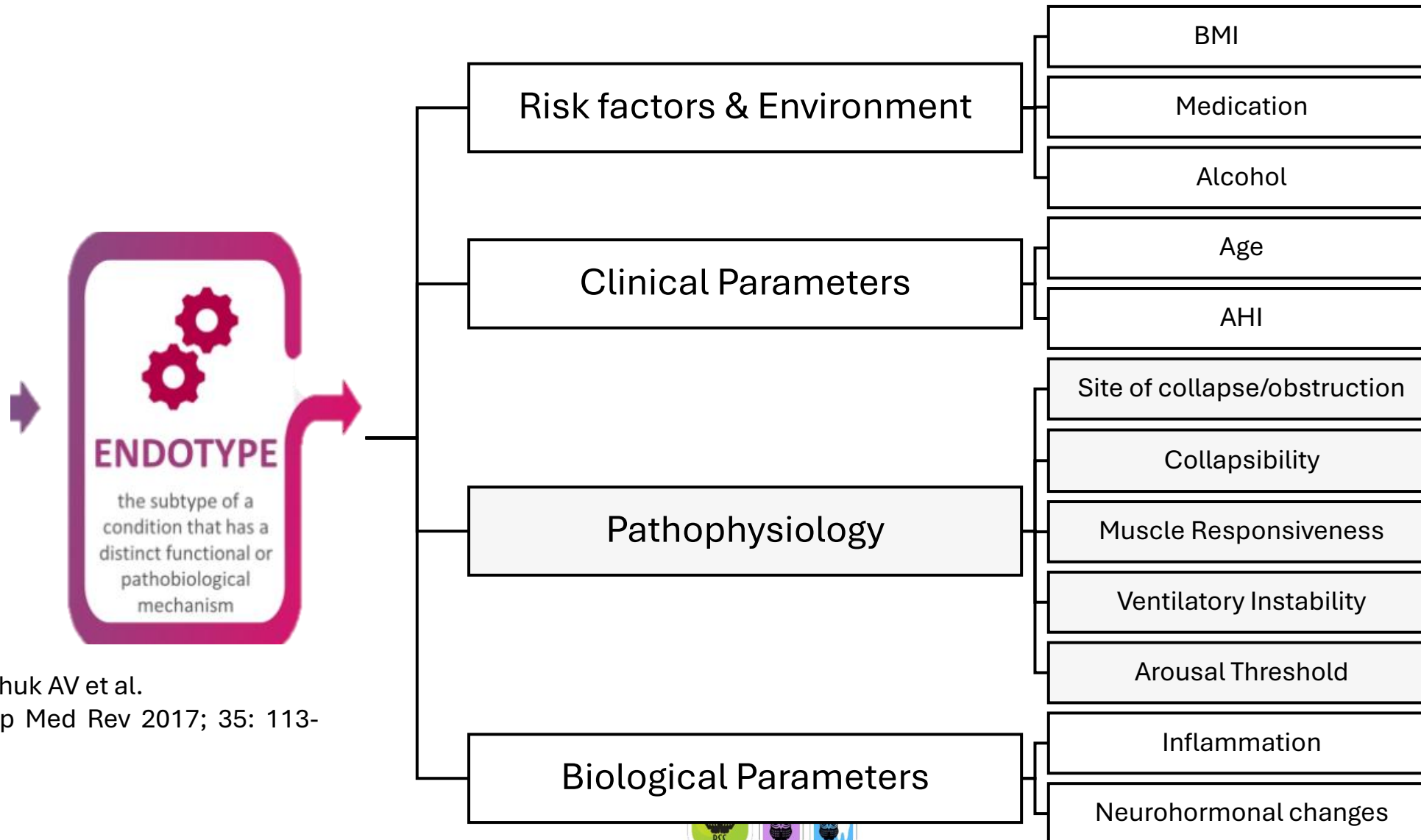
Morrell MJ et al Am J Resp Crit Care Med 1998;158:1974–81

Cross
sectional
area



Morrell M et al AJRCCM 1998;158:1974-81

Categorisation of OSA



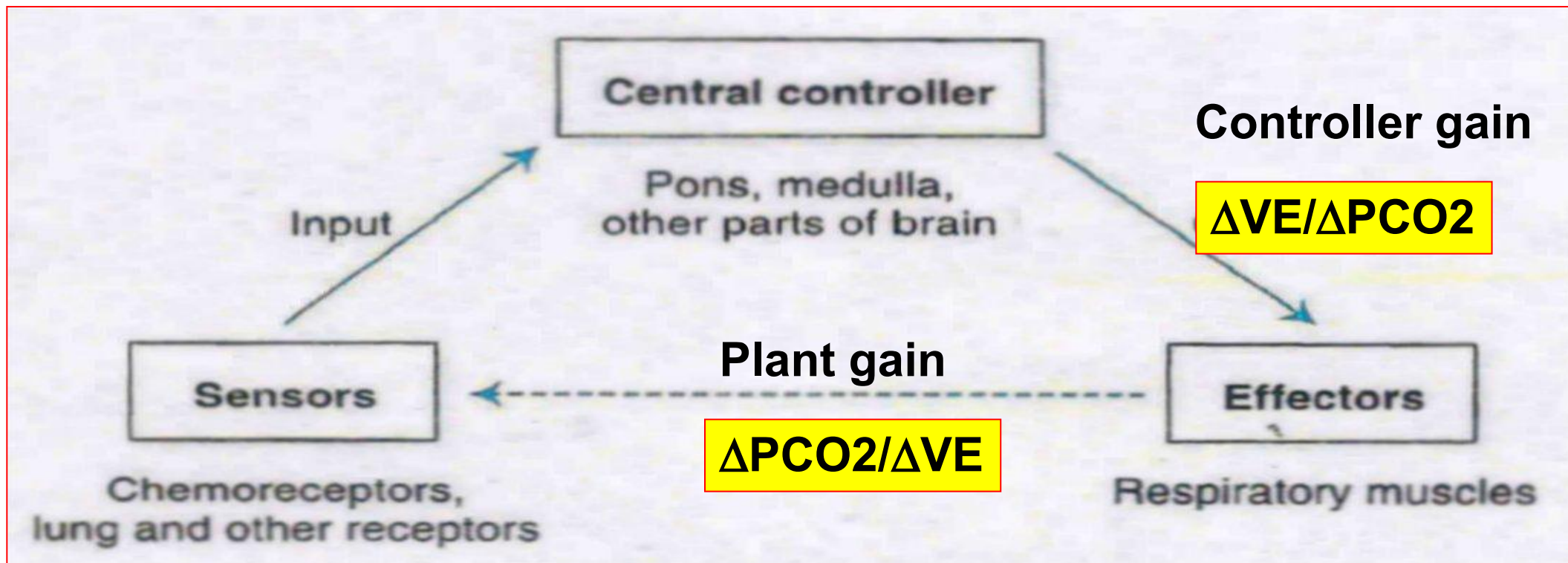
Zinchuk AV et al.
Sleep Med Rev 2017; 35: 113-23.

Mechanisms promoting periodic breathing and CSA

- Depressed central drive
- Increased O_2 (HVR) and CO_2 drive (HCVR)
- Unmasking of CO_2 threshold
- Stage effects
- Upper airway reflexes

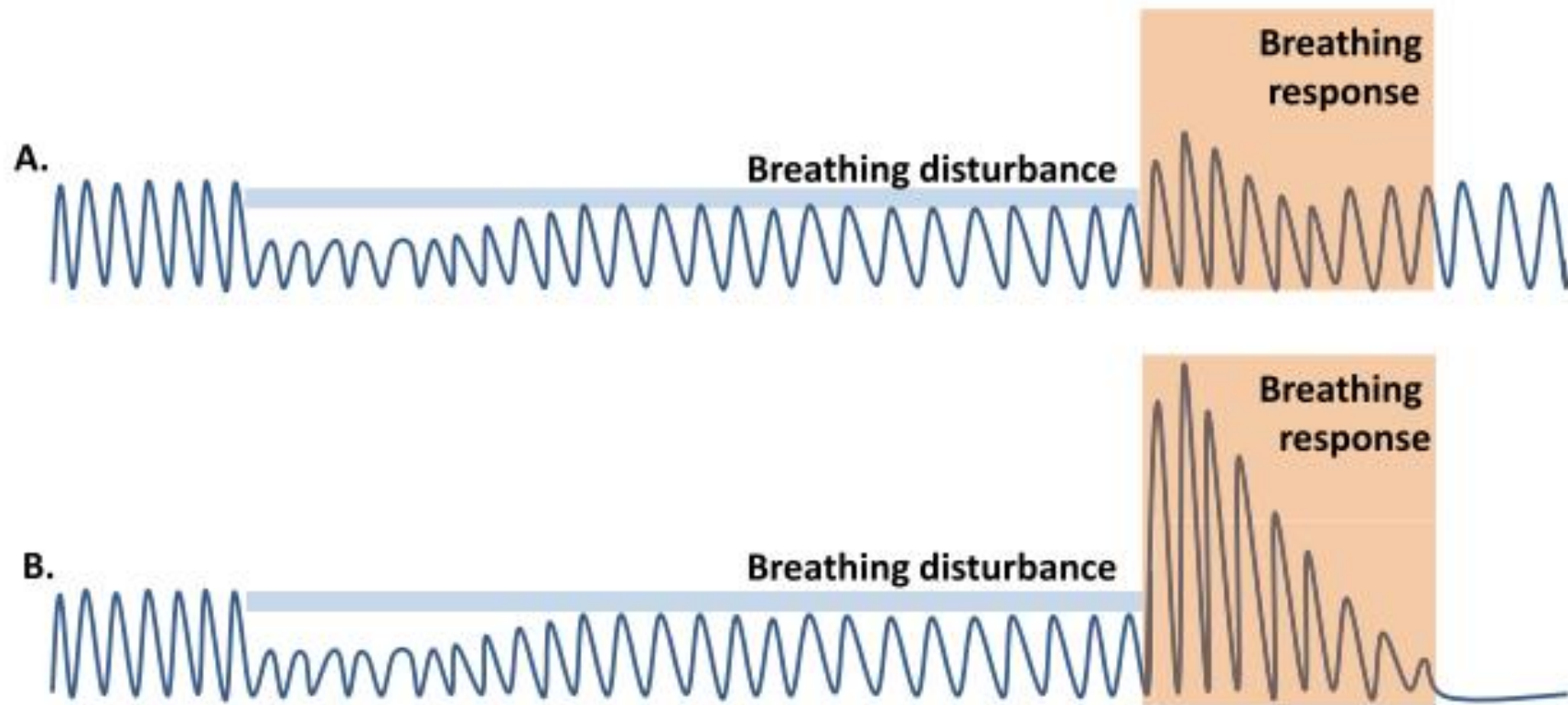
Pathogenesis periodic breathing/CSA

Instability in the respiratory control system



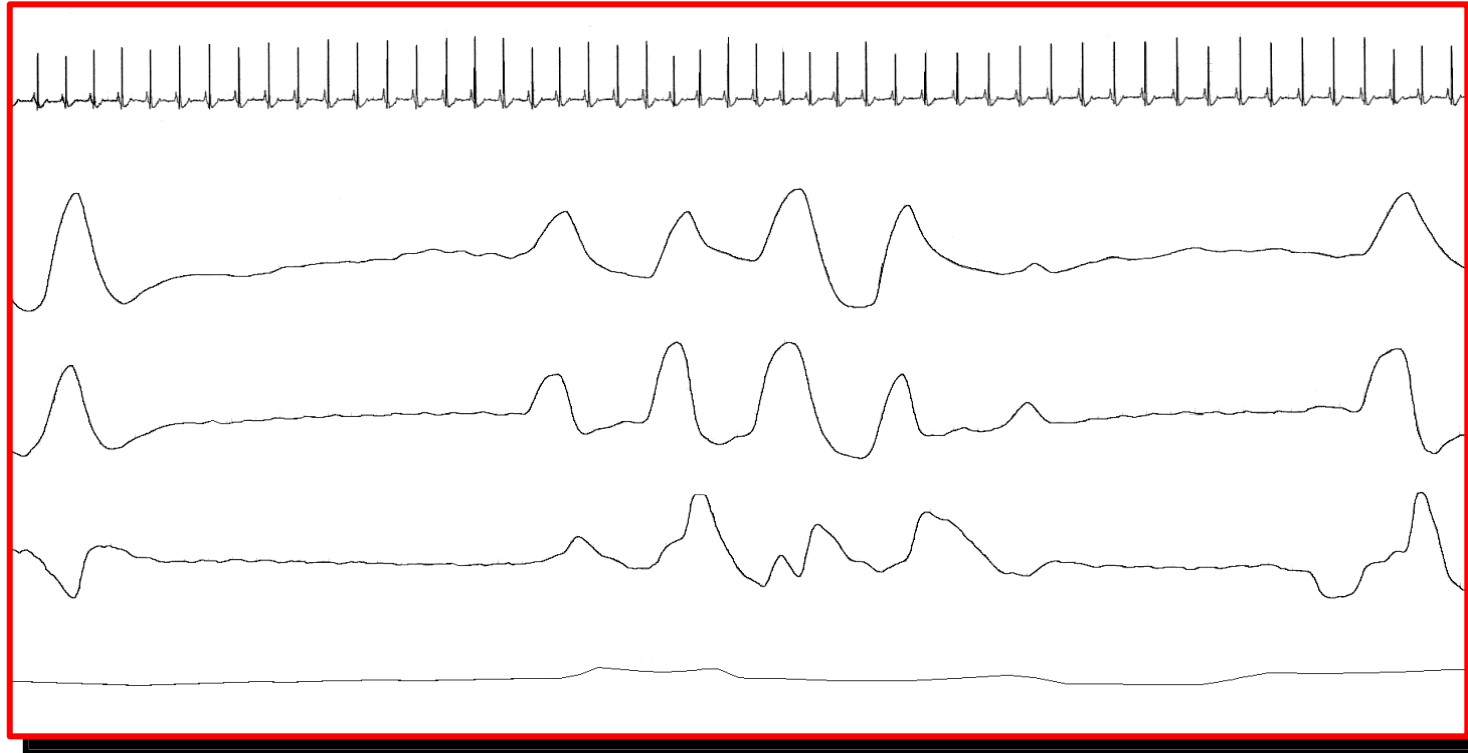
Pathogenesis periodic breathing/CSA

Post-apnoeic hyperventilation



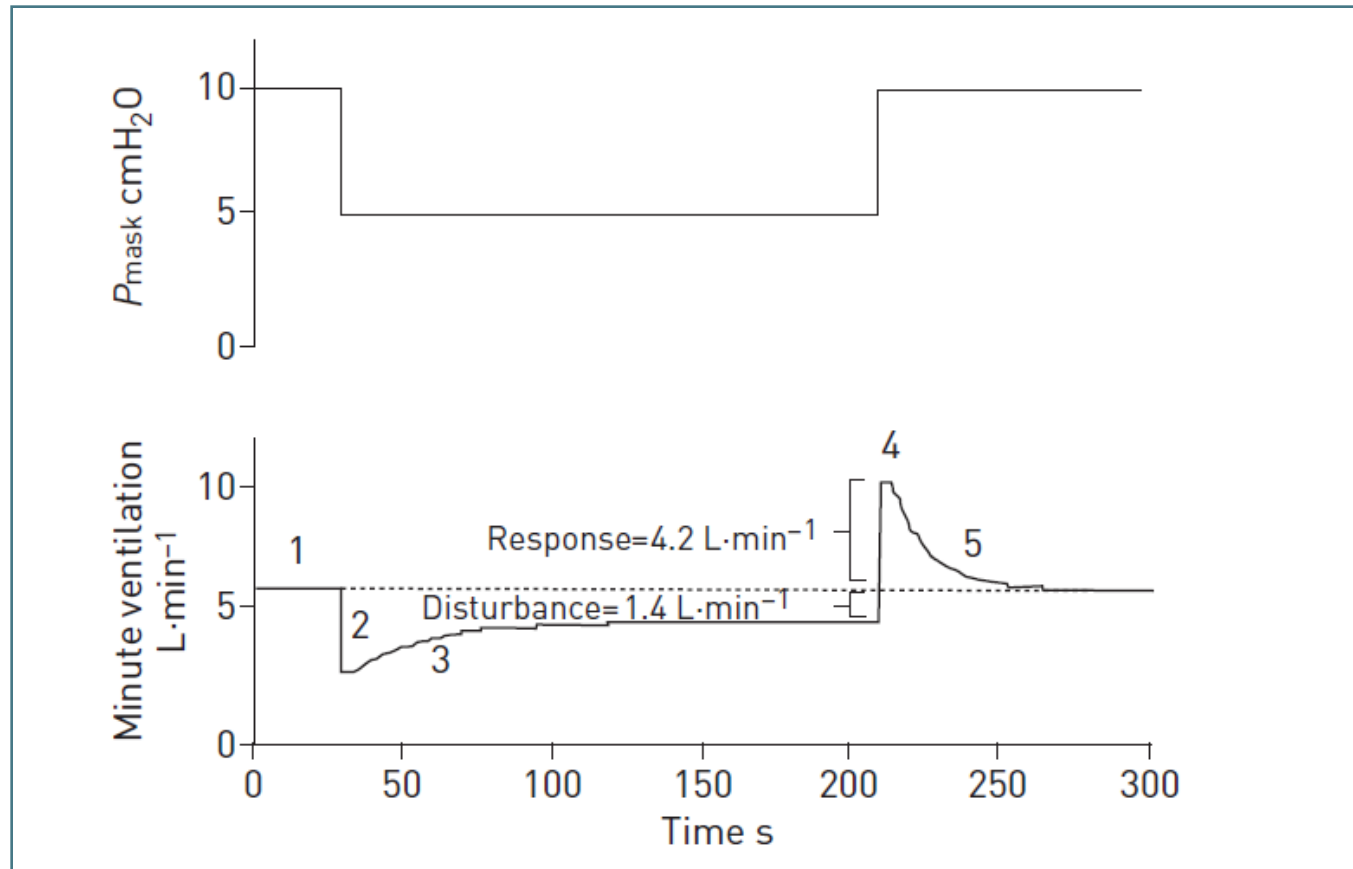
Eckert D. Sleep Med Rev 2018;37:45-59

Central apnoea



Berry RB. AASM Scoring Manual 2.5 (2018)

Measurement loop gain

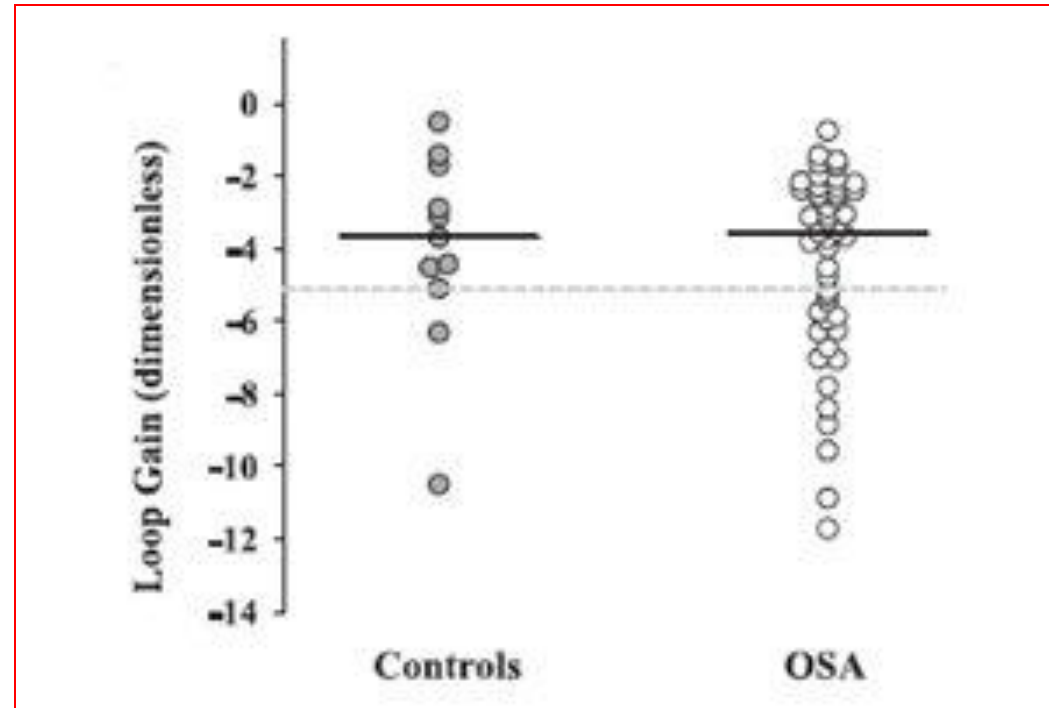


$$4.2 / -1.4 = -3$$

Loop gain:
the ratio of
ventilatory
overshoot to
the preceding
reduction in
ventilation

Wellman A et al JAP 2011;110:1627-37

Distribution loop gain



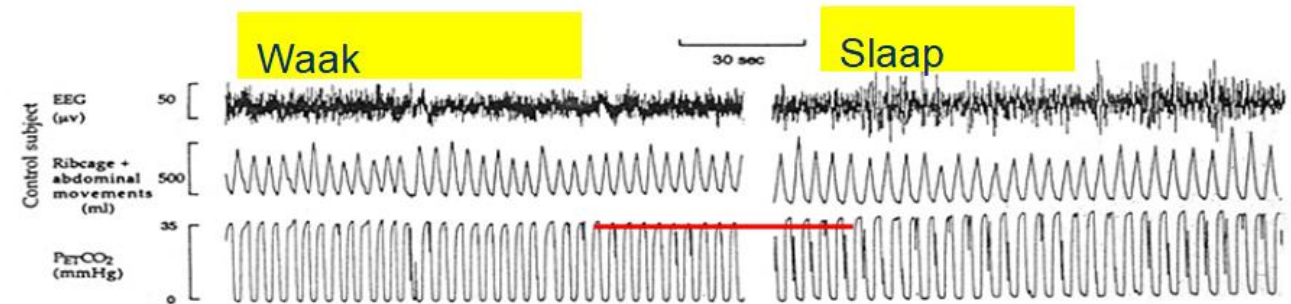
Eckert D et al AJRCCM 2013;188(8):996-1004

Pathogenesis periodic breathing/CSA

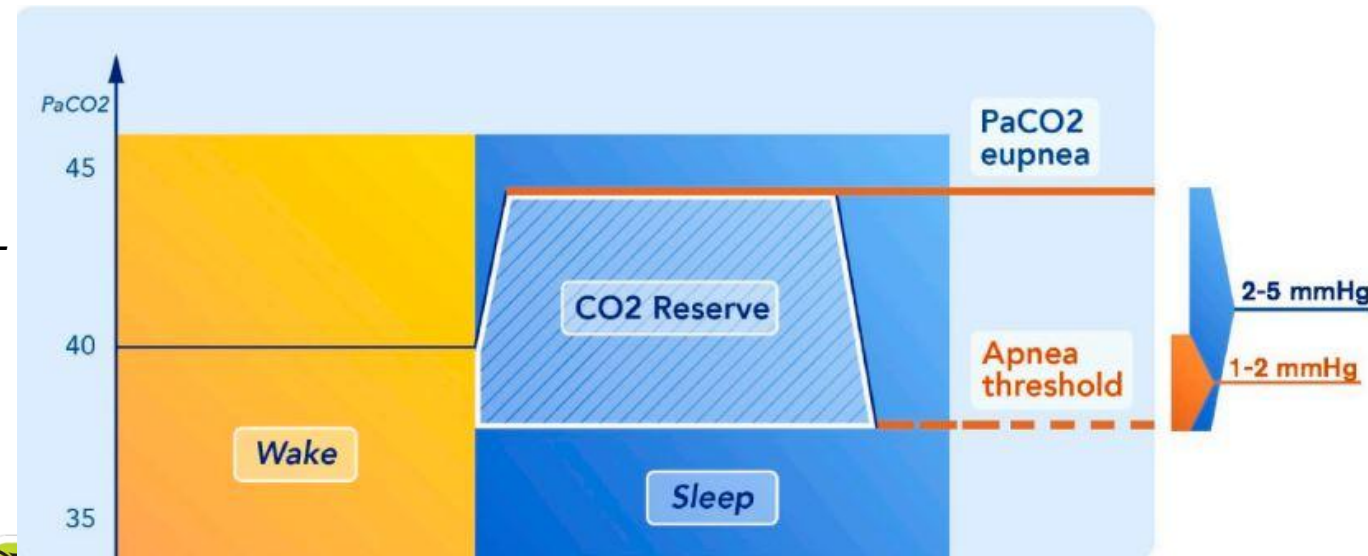
Activation of the CO₂ threshold (“apnoeic threshold”)

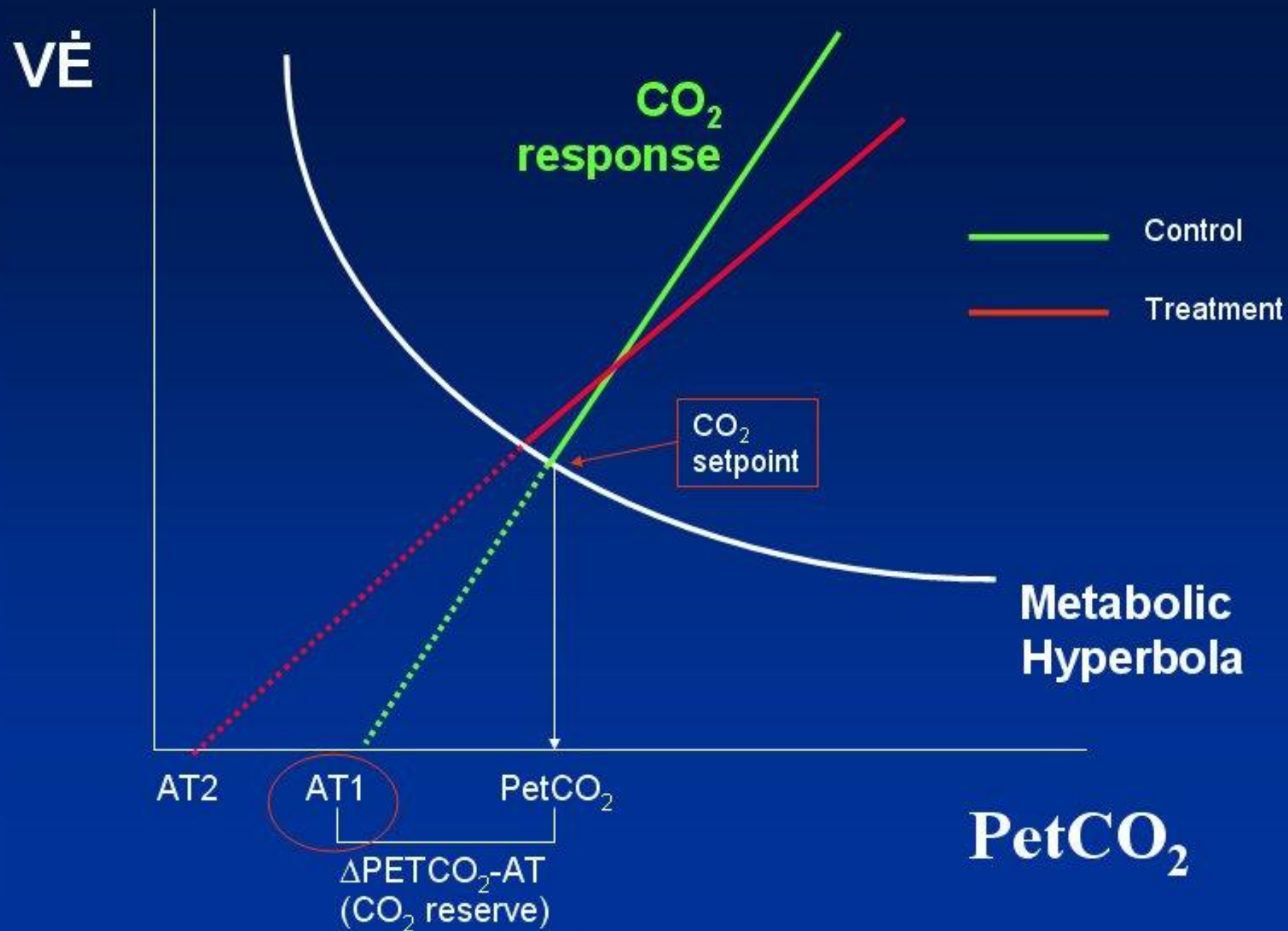
26

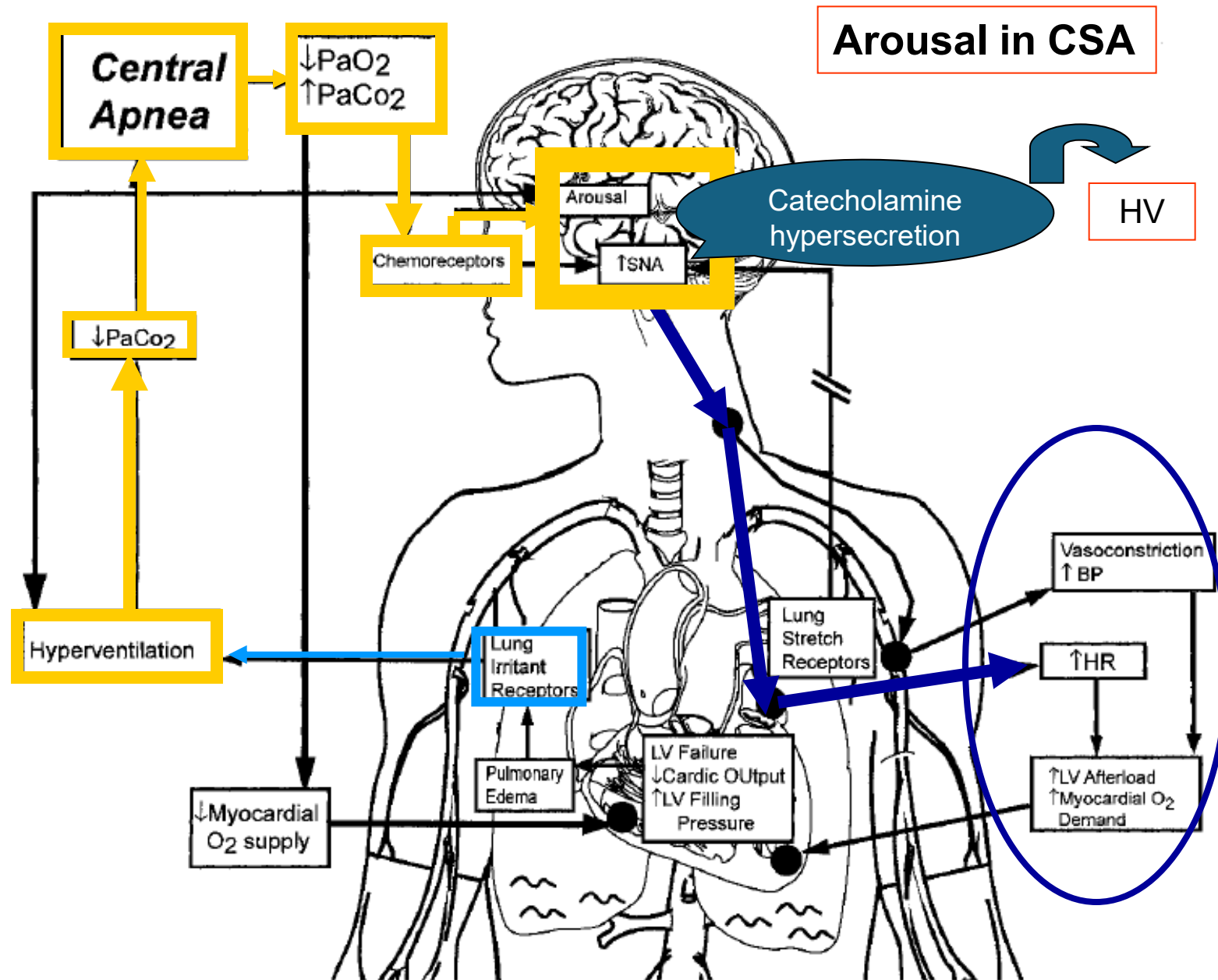
- PaCO₂ rises due to the sleep-induced rise in *Ruaw*.
- CA occurs after hyperventilation during sleep when PaCO₂ drops below a certain level (*apnoeic threshold*)
- PaCO₂ increases due to the sleep-induced *increase in Ruaw*. This *protects* subjects against central apnoeas since PaCO₂ remains (longer) above the apnoeic threshold
 - Skatrud et al *J Appl Physiol* 1983;55:813-22
 - Dempsey et al *Am Rev Respir Dis* 1986;133:1163-70



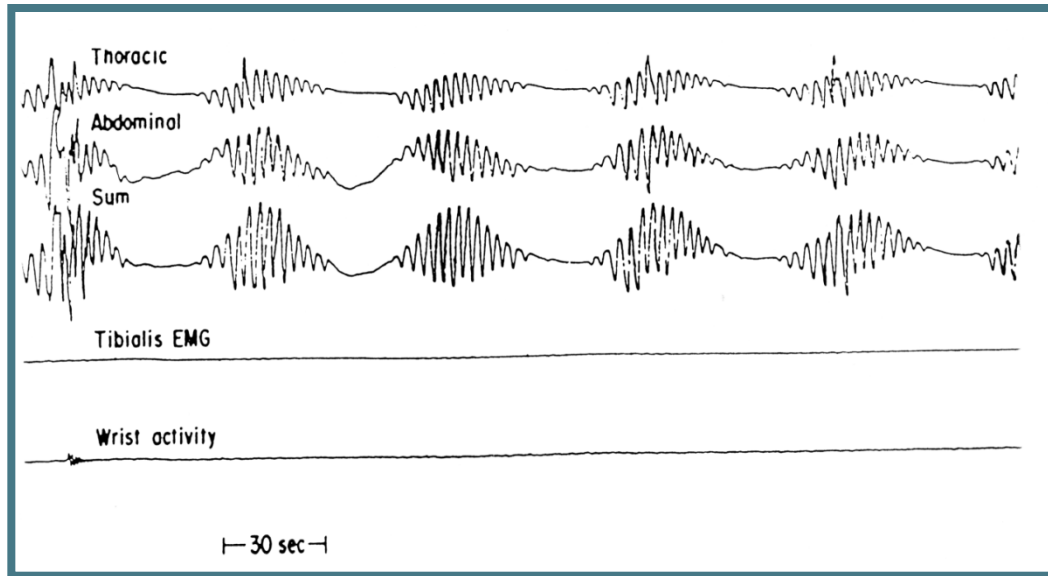
(Morrell et al. *J.A.P.* 1996;81:274-281)







Cyclic crescendo and decrecendo change in breathing amplitude ("waxing and waning")

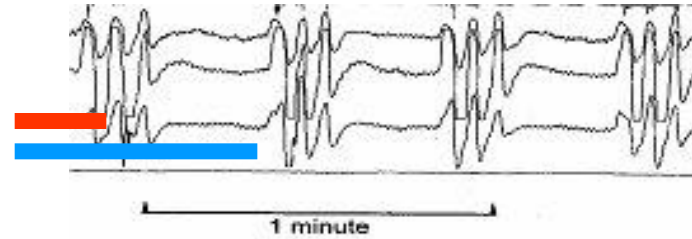


Quaranta AJ et al
Chest 1997;111:467-73

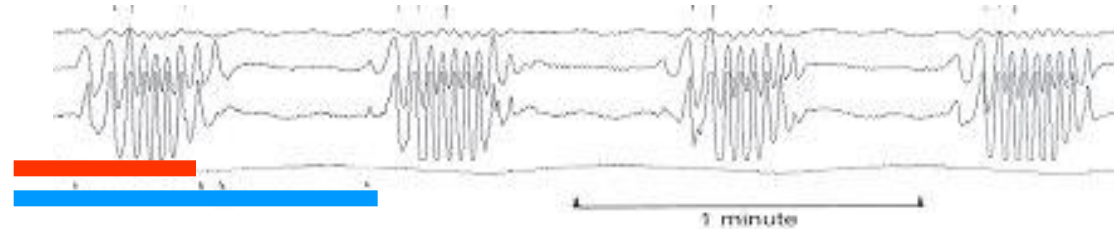
- CAHI $\geq$ 5
- Crescendo-decrecendo pattern
- Cycle period 40 to 90s
- Minimal registration time 2h

ICSD-3

Idiopathic CSA or Cheyne-Stokes ?



ICSA



CSR

Central apnoea

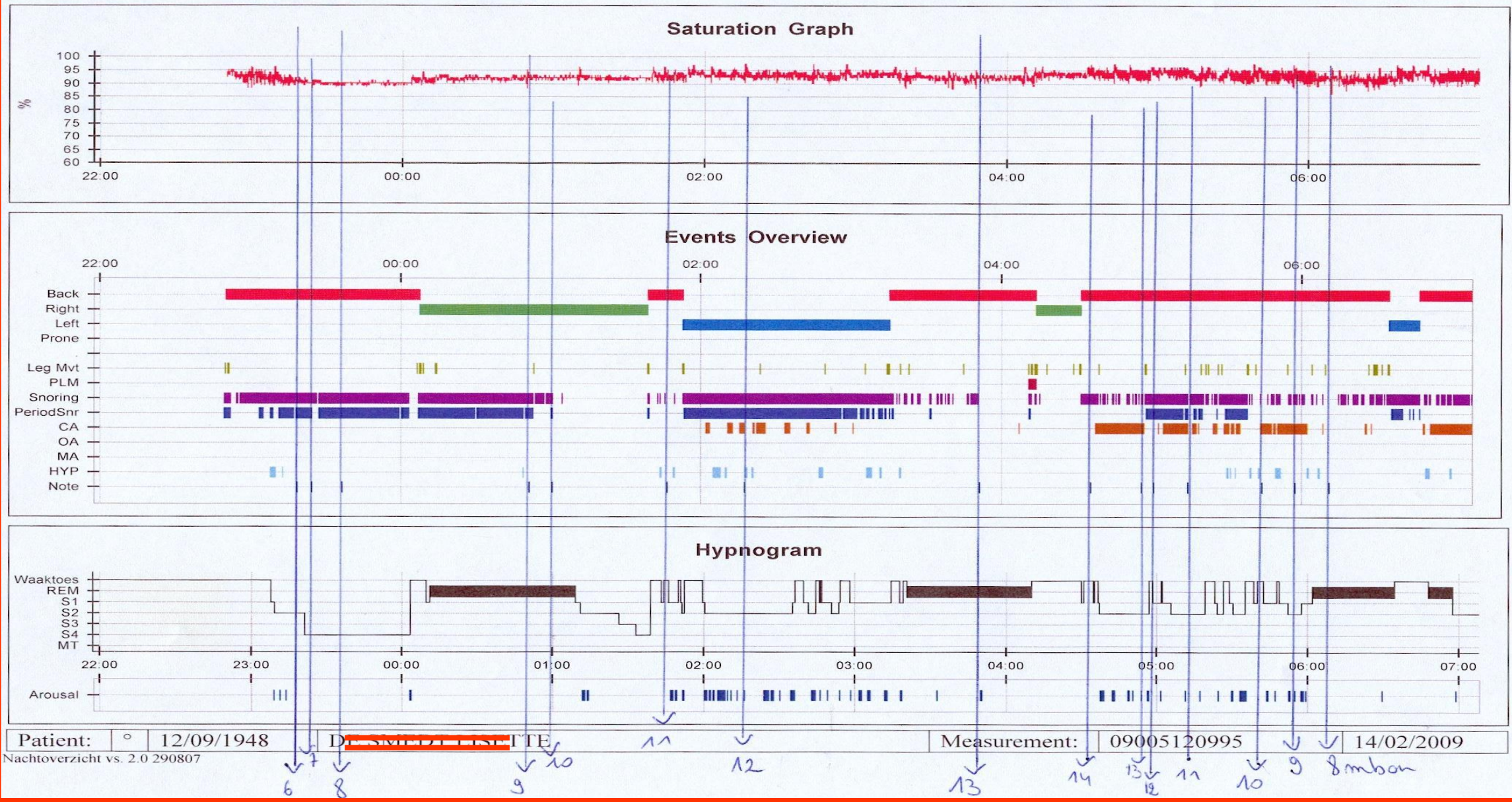
Subcategories(international classification)

- Central Sleep Apnea with Cheyne-Stokes Breathing (CSB)
- Central Apnea Due to a Medical Disorder without CSB
- Central Sleep Apnea Due to High Altitude Periodic Breathing
- Central Sleep Apnea Due to a Medication or Substance
- Primary Central Sleep Apnea
- Primary Central Sleep Apnea of Infancy
- Primary Central Sleep Apnea of Prematurity
- Treatment-Emergent Central Sleep Apnea (TECSA)

Central apnoea

Subcategories: Treatment-emergent CSA (TECSA)

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Central apnoea

Subcategories: opioid-induced central apnoea

Ataxic breathing → cluster breathing
(=variable amplitude, without any rhythm)



Quantification: variability in frequency and tidal volume

Mild=predominantly mild to **occasional** moderate variability

Moderate: clearly present throughout the largest part of the night.

Severe: severe variability throughout almost the whole night.

Variable apnoea duration !

Farney RJ et al J
Clin Sleep Med
2008;4:311-319

Dose-dependent:

equivalent of >200 mg → OR 15.4
mg; 61% if <200 mg.

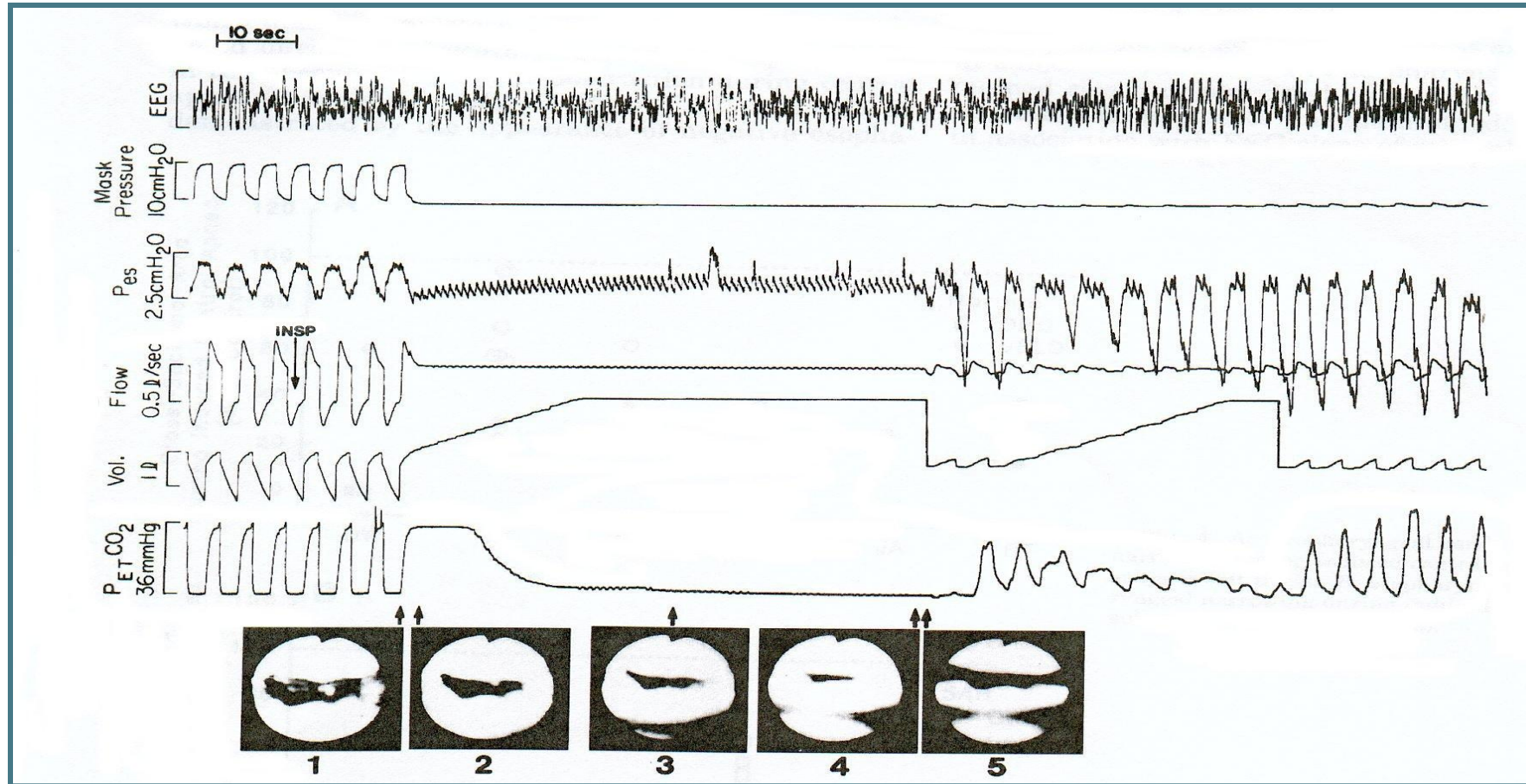
- morphine

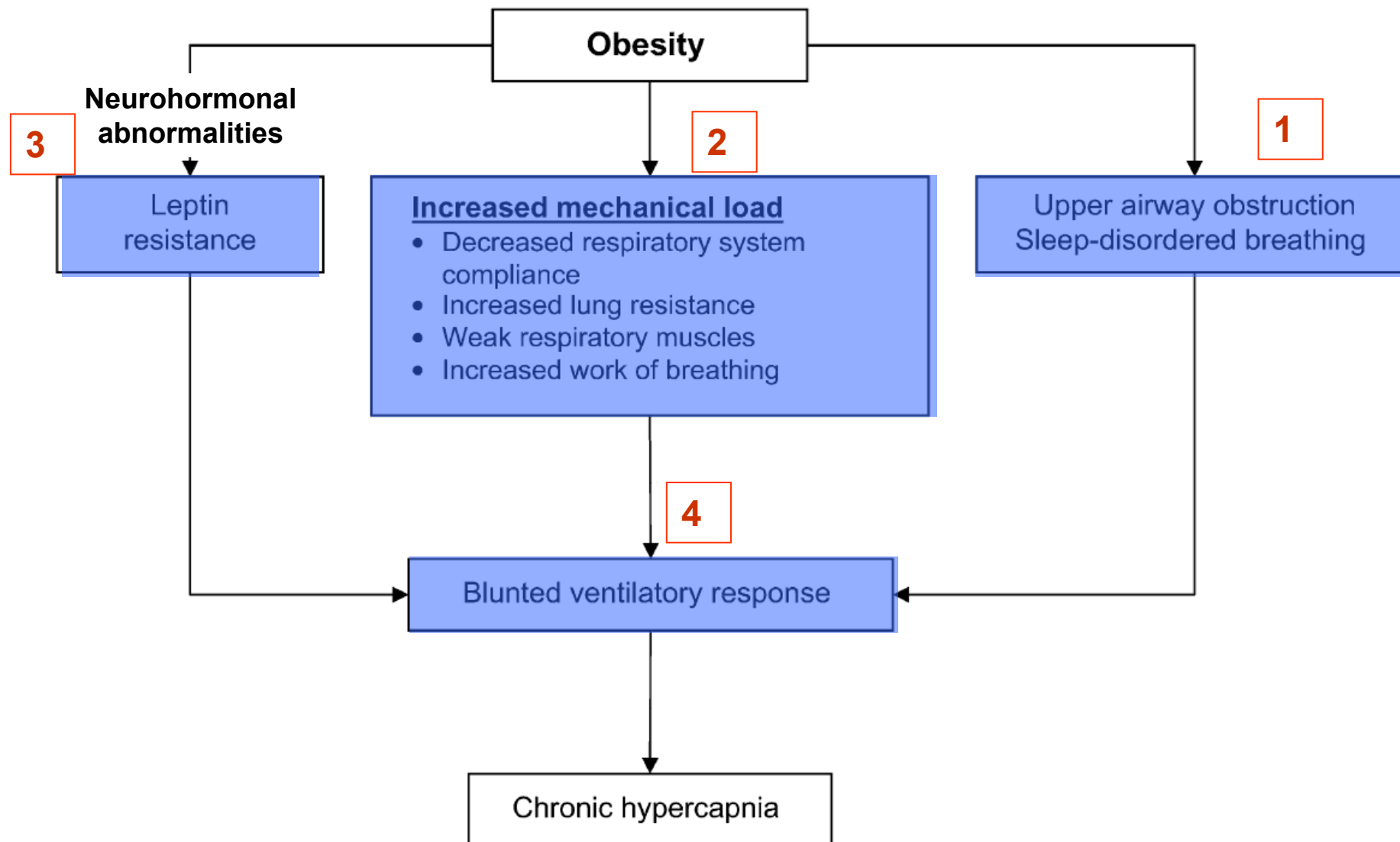
- in 92% if >200

- In methadone users: 30-60%

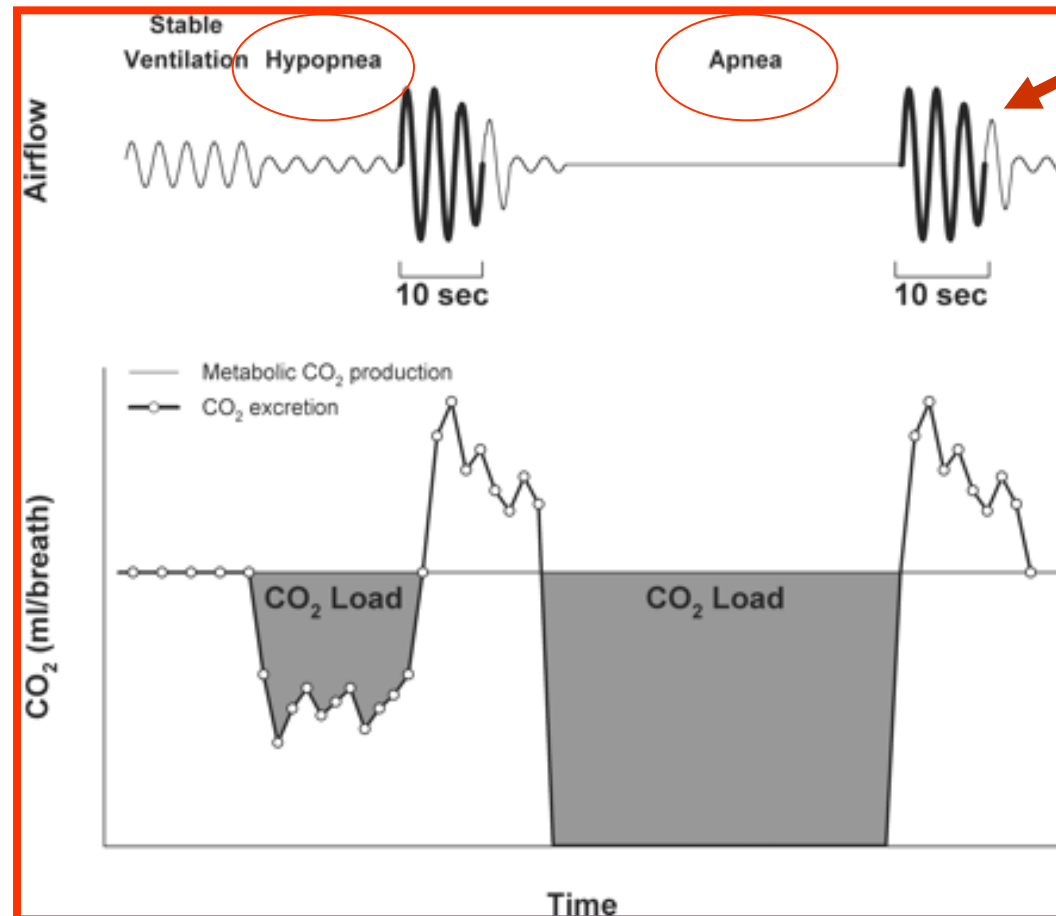
Decrease dose narcotics, alternative analgesics !

Pathogenesis of central apnoea open or closed airway ?





Imbalance between CO₂ load during respiratory events and post event ventilation



Magnitude and duration of post event ventilation: inadequate duration of hyperventilation

Acute hypercapnia causes a small $\uparrow$ in serum bicarbonate level, which blunts the HCVR.

CONCLUSIONS

- OSA: the pathogenesis is complex but increased *collapsibility* of the upper airway and *increased instability* of the breathing pattern *both* are contributing factors.
- Endotyping in OSA (“traits”): the weight of the different pathophysiological mechanisms may vary in individual patients: useful targets for therapy.
- CSA and CSA-CSR: can predominantly be explained by increased chemical drive and activation of the CO₂ threshold
- OHS: Increased *mechanical load*, but it does not appear that obesity is the only determinant of OHS as only a minority of morbidly obese patients develops chronic hypercapnia

Reference

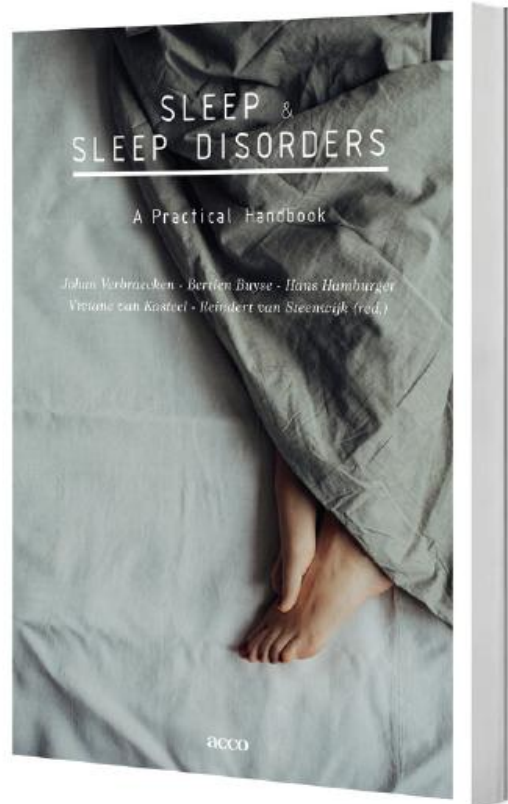


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SERIES
J. VERBRAECKEN ET AL.

The upper airway in obstructive sleep apnoea: state of the art

Johan Verbraecken ^{1,2}, Sara Op de Beeck ^{3,4}, Alan R. Schwartz^{5,6,7} and Olivier M. Vanderveken ^{2,3,4}

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