

Ventilatory Control and Airway Anatomy in OSA

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Obstructive sleep apnea

- An increasingly common sleep-related breathing disorder
- Repetitive apnea and/or hypopnea during sleep
- Intermittent hypoxia, hypercapnia, and frequent cortical arousals
- Adversely affects cardiovascular system, cause neurocognitive impairment, daytime sleepiness, and increase the risk of motor vehicle accidents

Obstructive sleep apnea pathogenesis

Anatomical components

Narrow, crowded, collapsible upper airway

Non-anatomical components

Ventilatory control instability
Low respiratory arousal threshold
Reduced pharyngeal dilator muscle activity

Contents

- 1. The upper airway anatomy**
- 2. Ventilatory control stability**
- 3. Anatomical factors contributing to OSA**
- 4. Ventilatory control in OSA**

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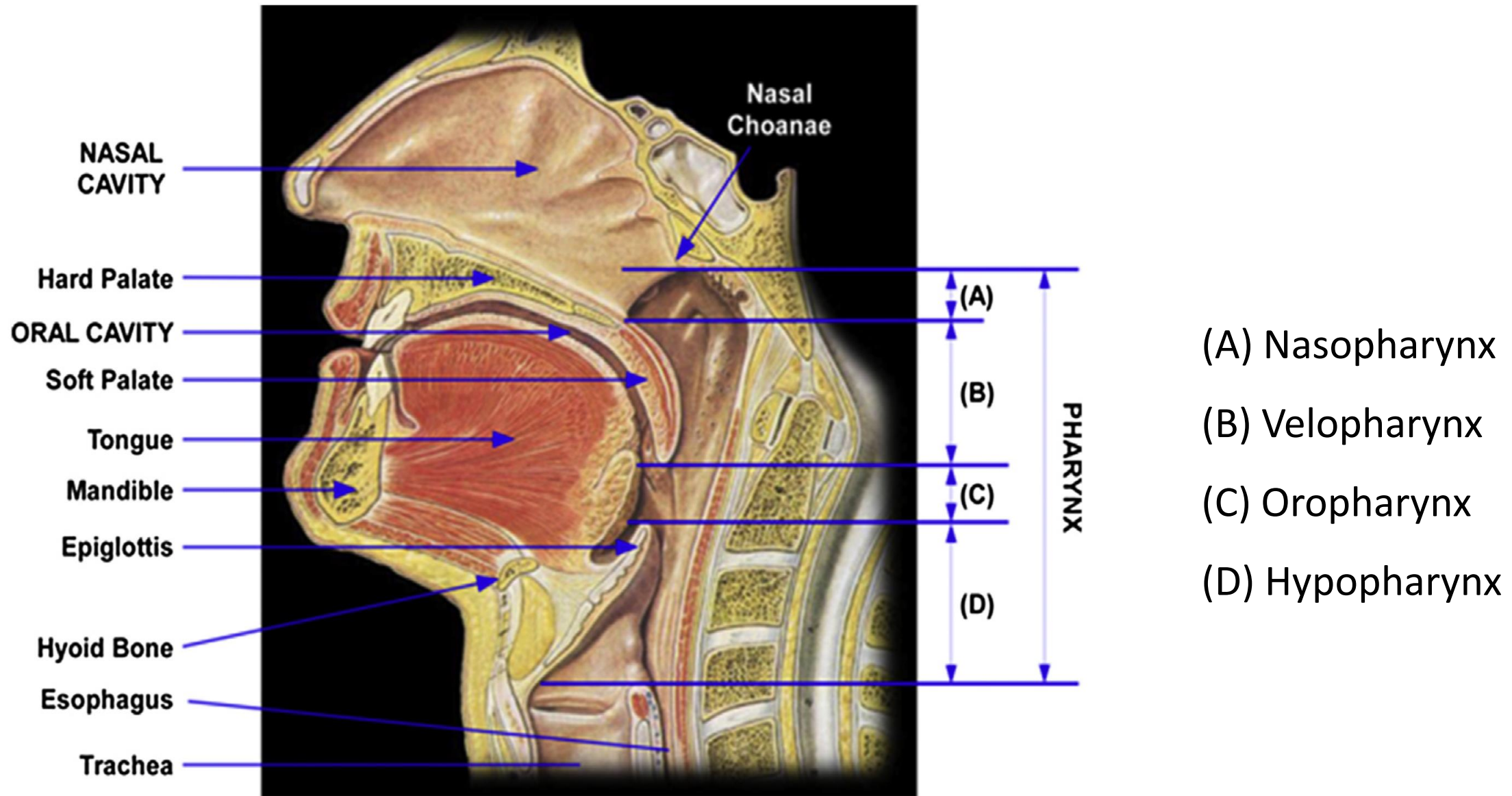
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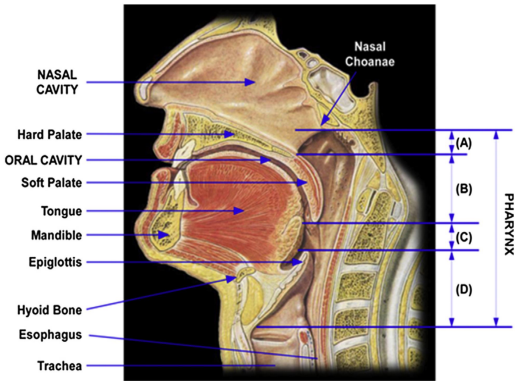
The upper airway

- A tube starting at the nasal choanae and ending at the vocal folds
- A unique multipurpose structure

- passage of air for breathing
- heating and humidification of air
- speech
- swallowing of food/liquids

An intricate arrangement of **soft** (24 muscles and other soft tissues), **cartilaginous** (thyroid cartilage, epiglottis), and **bony** (hard palate, mandible, and hyoid bone) tissues





Nasopharynx

From the posterior nasal choanae to the caudal margin of the hard palate

Velopharynx

From the cranial to caudal margin of the soft palate

Oropharynx

From the tip of the soft palate to the tip of the epiglottis

Hypopharynx

From the cranial margin of the epiglottis to the glottis

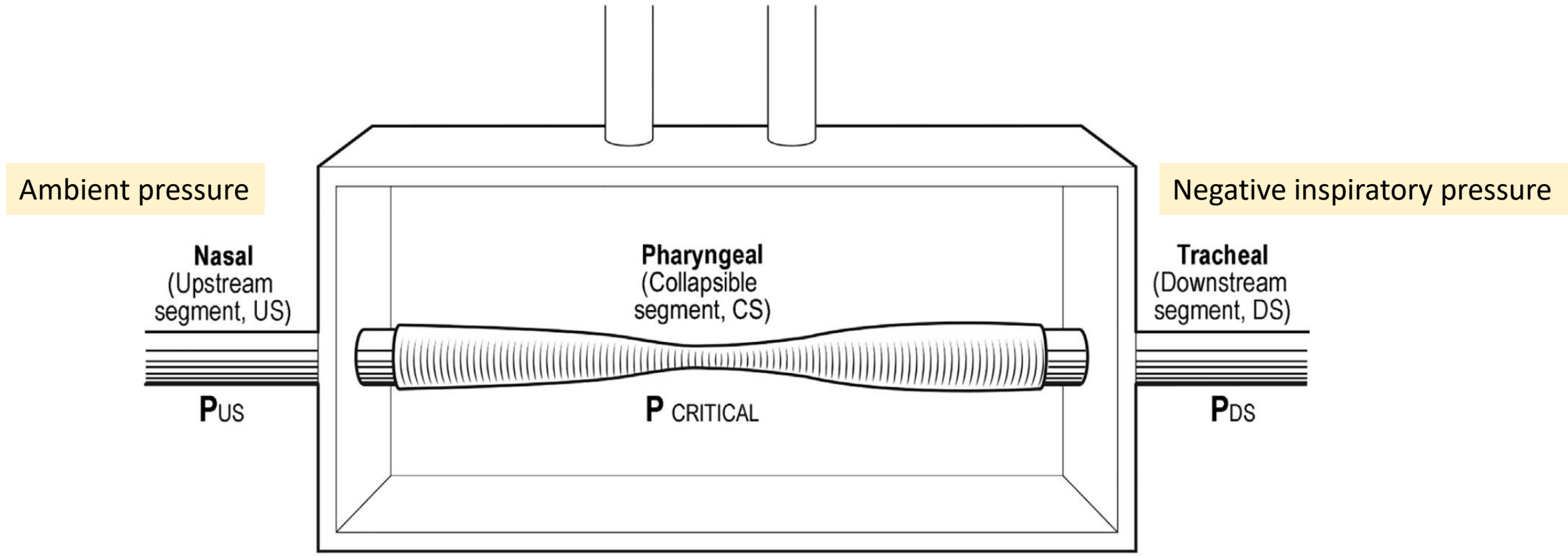
The upper airway

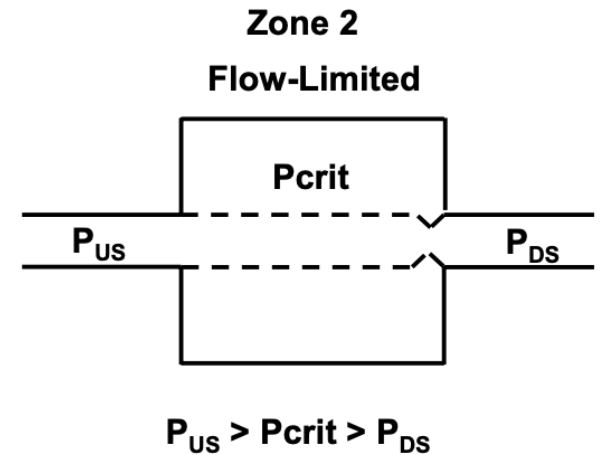
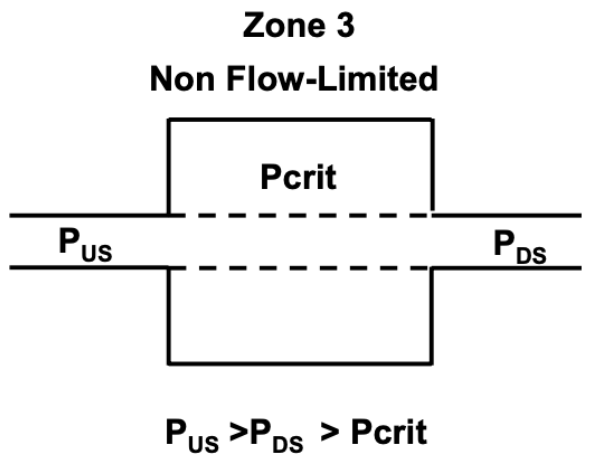
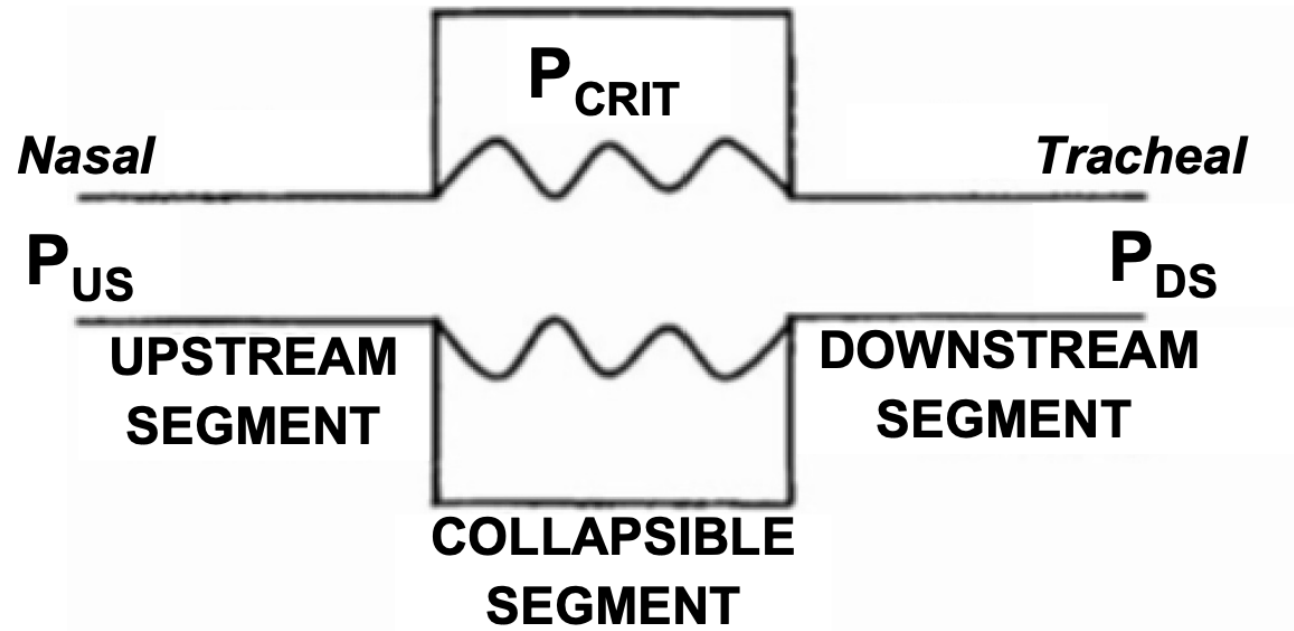
No bony or cartilaginous support except for the posterior vertebral column

→ **Highly deformable** and **prone to collapse** during sleep

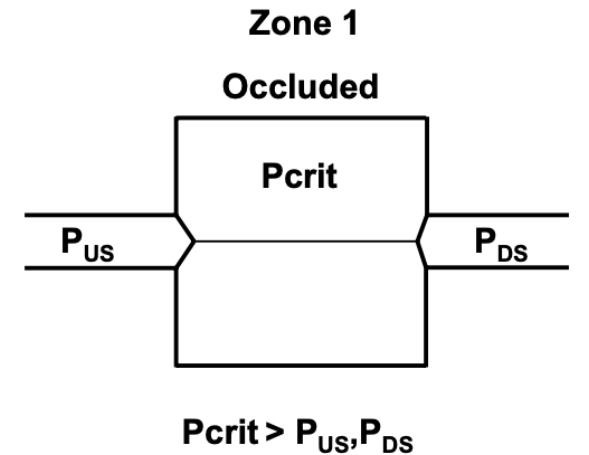
The most collapsible region is the the **velopharynx** followed by the **oropharynx**

Starling resistor model



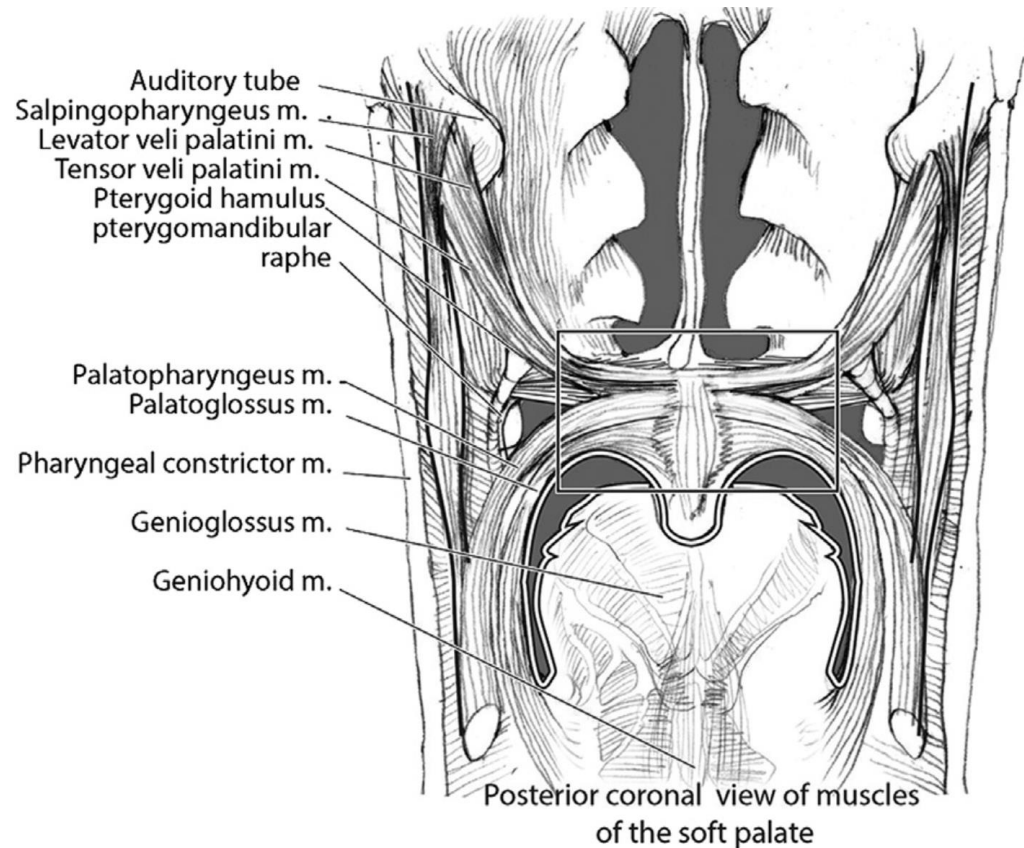
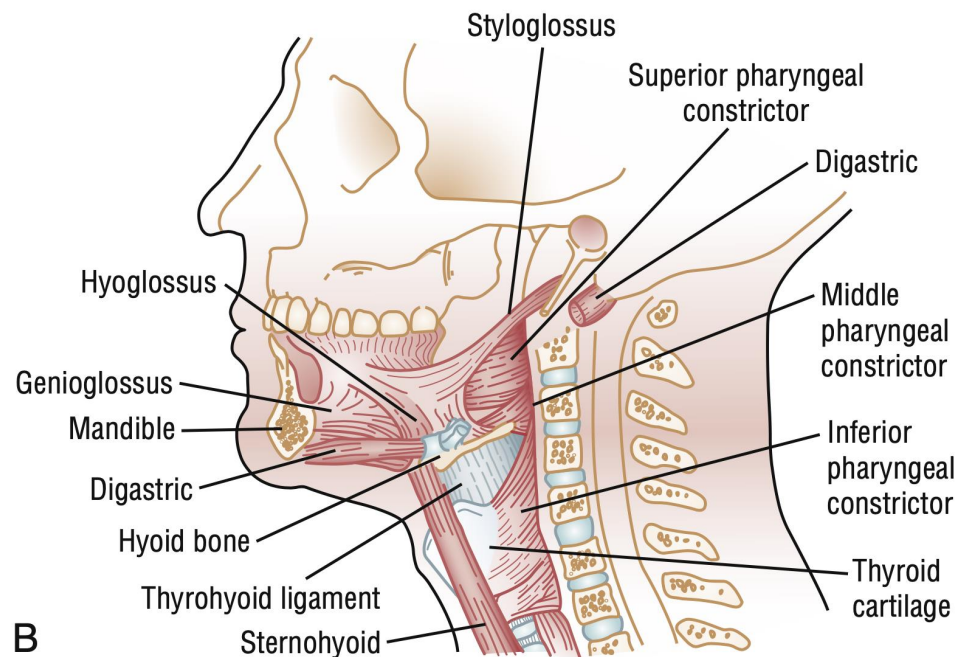


$$V_{I,max} = (P_{US} - P_{crit}) / R_{US}$$



Upper airway muscles

- Regulate the position of the soft palate, tongue, hyoid bone, and pharyngeal wall
- Control major functions of the upper airway such as phonation and swallowing



Pharyngeal dilator muscles

1) Tonic (constant) activity

Independent of phase of respiration

e.g., tensor veli palatini

2) Phasic activity

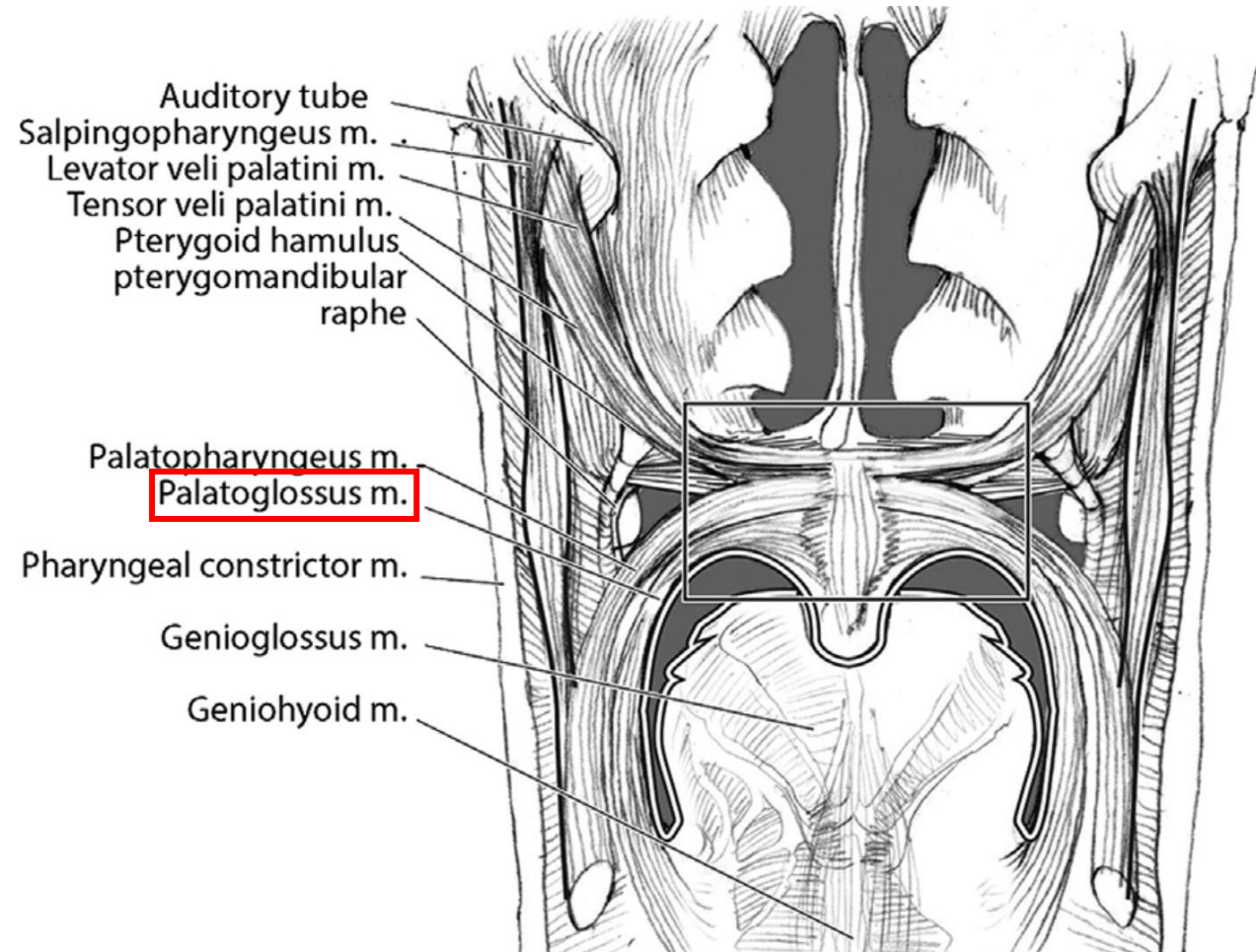
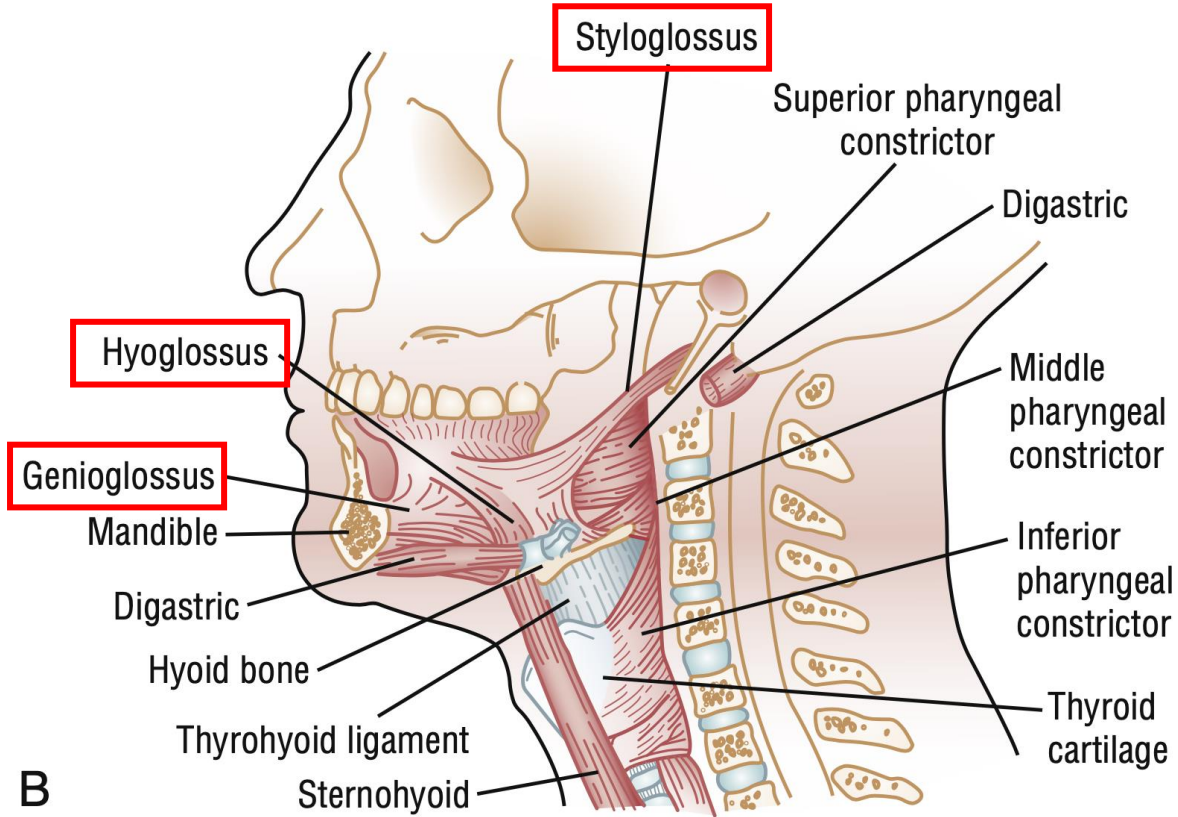
occurring during one part of the respiratory cycle

e.g., genioglossus

Activity of upper airway dilators begins about 200 msec before onset of thoracic pump activity in normal subjects

Upper airway muscles

4 extrinsic tongue muscles



Upper airway dilator reflex responsiveness

- **Genioglossus negative pressure reflex**
 - **muscle activation** in response to rapid changes in **negative** intra-pharyngeal pressure
 - modulated by locally mediated mechanoreceptive reflex mechanisms that respond to negative pharyngeal pressure
- During sleep (NREM, REM) → **diminished reflex activation**

The upper airway and sleep

At the onset of sleep

- 1) Decrease in upper airway muscle activity
- 2) Decreased upper airway compliance
- 3) Smaller upper airway lumen size
- 4) Increased upper airway resistance
- 5) Decreased pharyngeal neurocompensatory reflex

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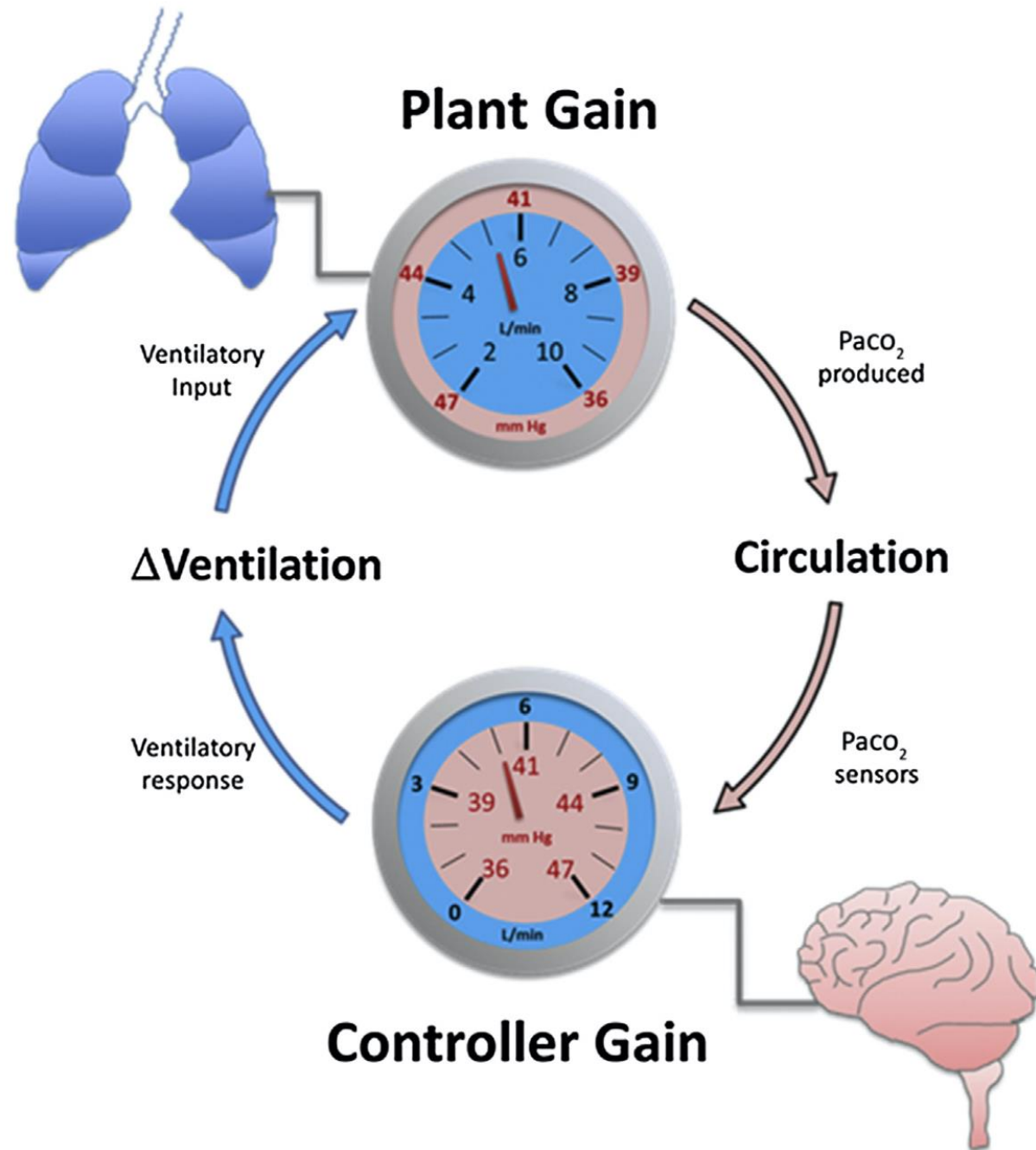
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Ventilatory control stability

Ventilatory control is tightly organized as a **negative feedback** system to maintain the $P_{a_{CO_2}}$

Ventilatory control stability (respiratory loop gain concept)

- 1) **Plant gain**
- 2) **Controller gain**
- 3) **Circulatory delay (mixing gain)**



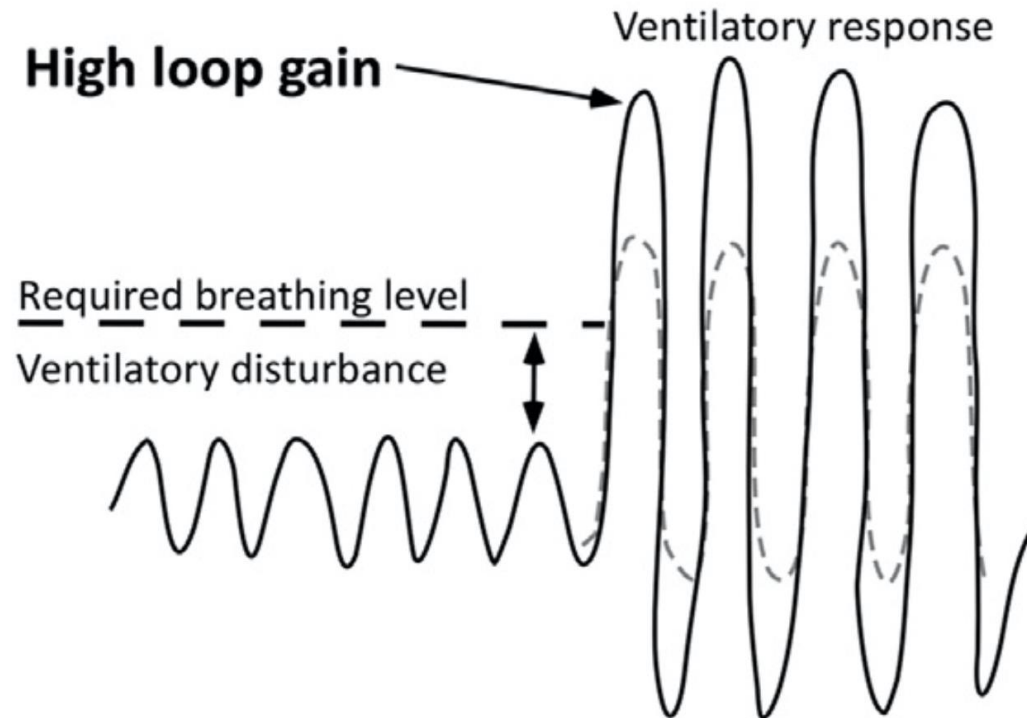
Loop gain

Respiratory plant	<ul style="list-style-type: none">• Refers to the lungs, body tissue, and blood where CO₂ is stored• Represented by the change in Pa_{CO₂} for a given change in ventilation $\Delta Pa_{CO_2}/\Delta V_E$• Performance depends on the mechanical and biochemical properties of its component (e.g., lung compliance, VQ matching, Hb concentration, etc.)
Circulatory delay	<ul style="list-style-type: none">• Transit time from the pulmonary capillaries to reach the central and peripheral chemoreceptors• Speed with which changes in Pa_{CO₂} and Pa_{O₂} from the plant are detected by the controller• A function of cardiac output
Central respiratory controller	<ul style="list-style-type: none">• Converts the signal from the chemoreceptors into a ventilatory drive for the plant• Response to the change in Pa_{CO₂} through negative feedback to appropriately change V_E (anticipated ventilation for a given Pa_{CO₂})• Represented by the change in V_E for a given change in Pa_{CO₂} $\Delta V_E/\Delta Pa_{CO_2}$

Respiratory loop gain

: a ratio of a ventilatory response for a given ventilatory disturbance

The overall loop gain (V_e response/ V_e disturbance) is the product of controller, plant, and mixing gains and determines how stable the respiratory system is.



Loop gain

High loop gain system

- Response with larger ventilatory changes to a given perturbation (e.g., apnea or hypopnea)
- More likely to become unstable

Low loop gain system

- Response with smaller changes in ventilation
- More inherently stable

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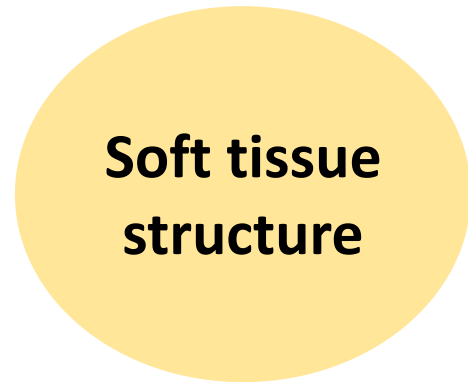
Pathophysiology of OSA

- Multifactorial
- Individual variability

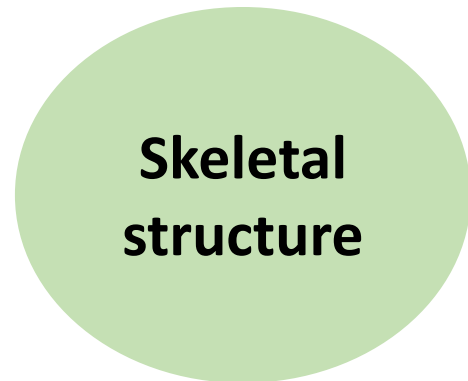
Complex interaction among pharyngeal dilator tone, arousal threshold, respiratory control instability, and changes in lung volume during sleep

Structural determinants of OSA

Two major structural determinants of OSA



Airway size, shape, and compliance
Size and position of the tongue, palate, and tonsils
Fat deposition within the pharyngeal wall



Skeletal framework of the face and neck
Mandible, maxilla, and hyoid bone

Anatomical factors contributing to obstruction

Lateral pharyngeal narrowing

Enlarged tonsils, soft palate, uvula, and tongue

Excessive parapharyngeal fat tissue

Small maxilla and mandible

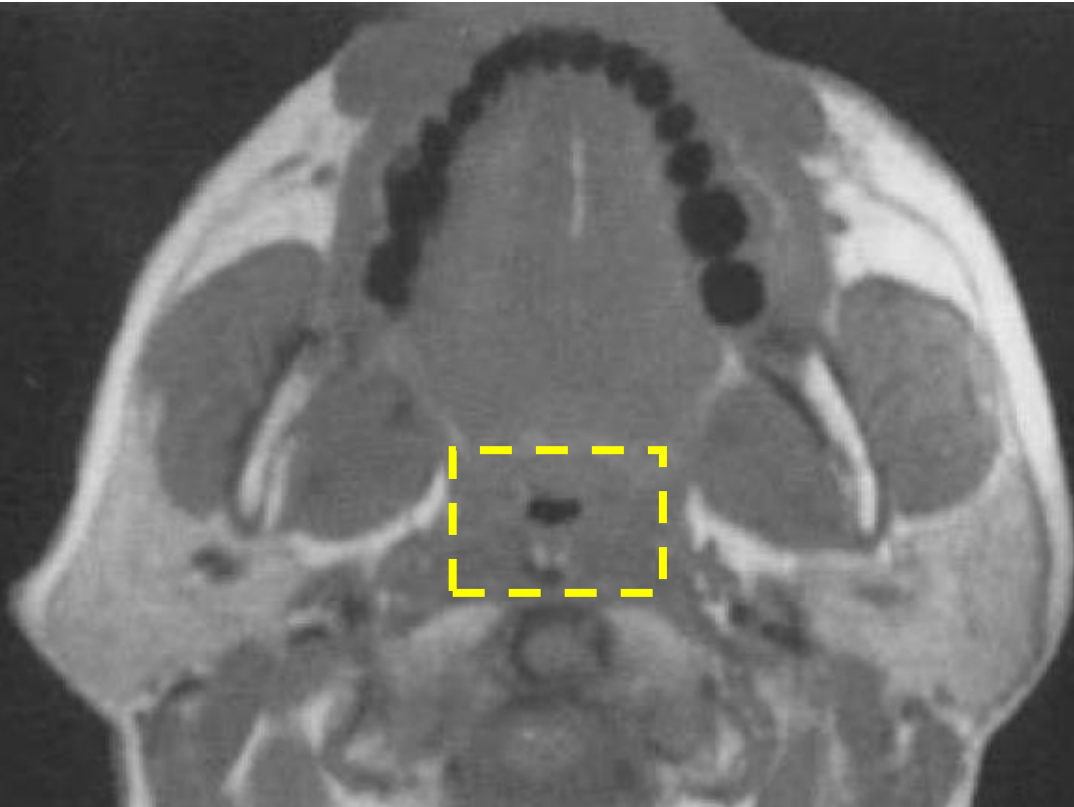
Increased vertical length of the upper airway

Increased distance between the hyoid and the mandibular plane

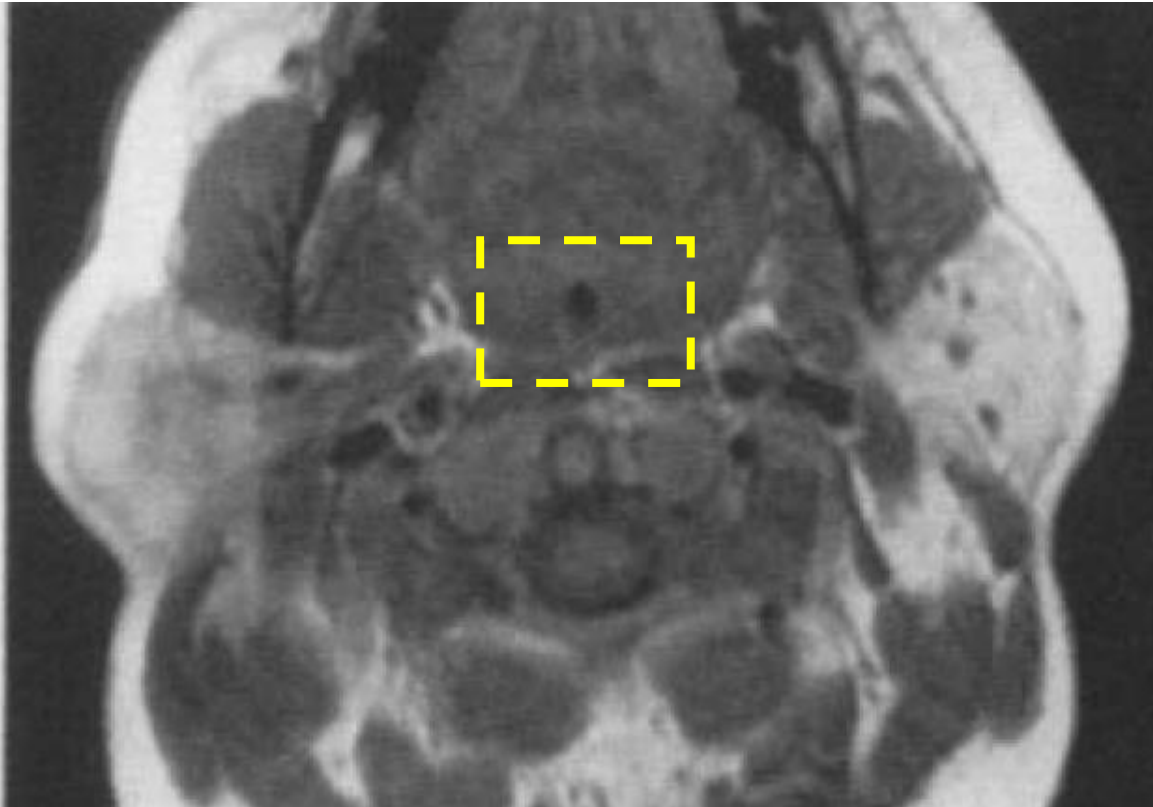
Decreased mandibular and maxillary projection

Increased cervical angulation

Narrow upper airway

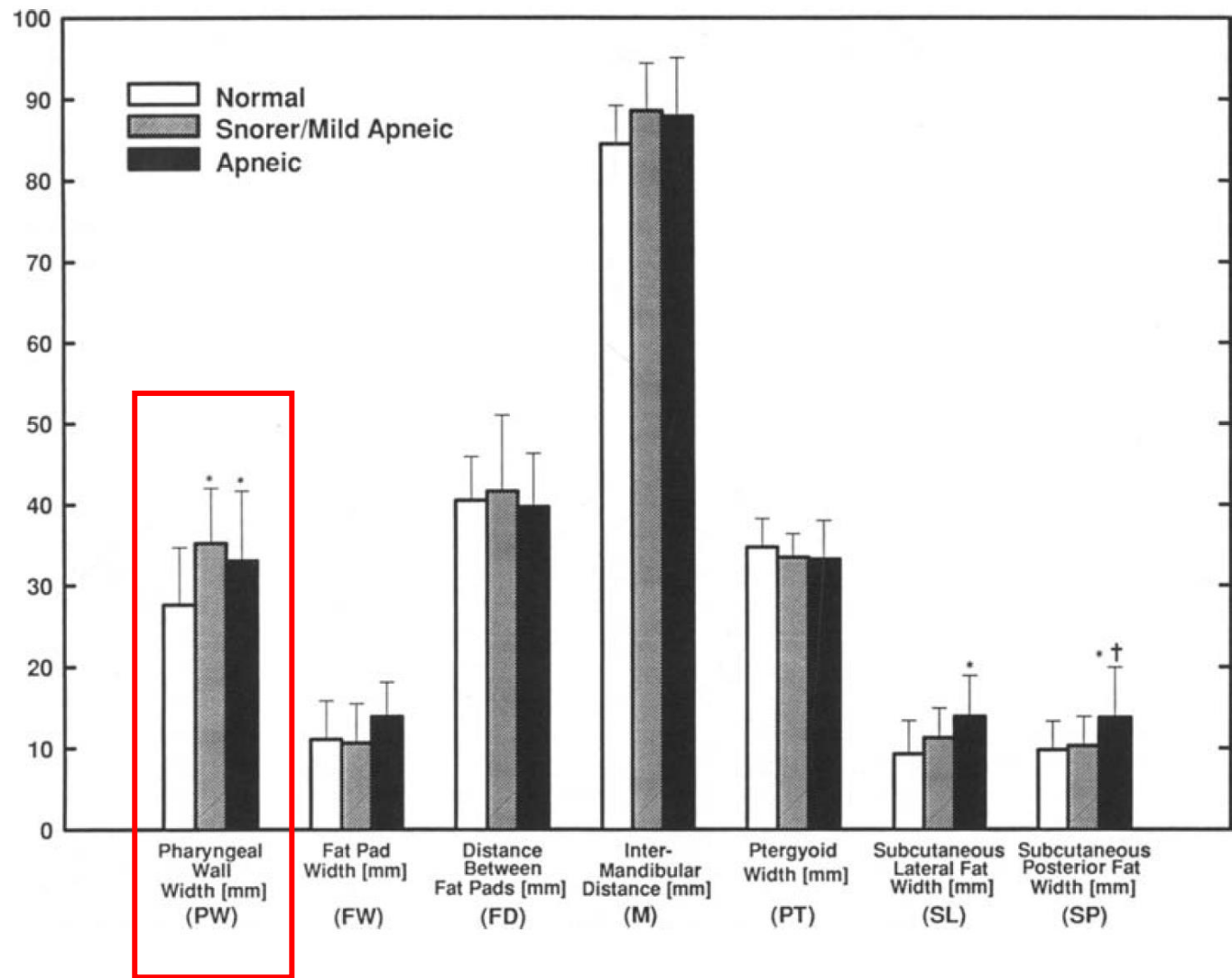
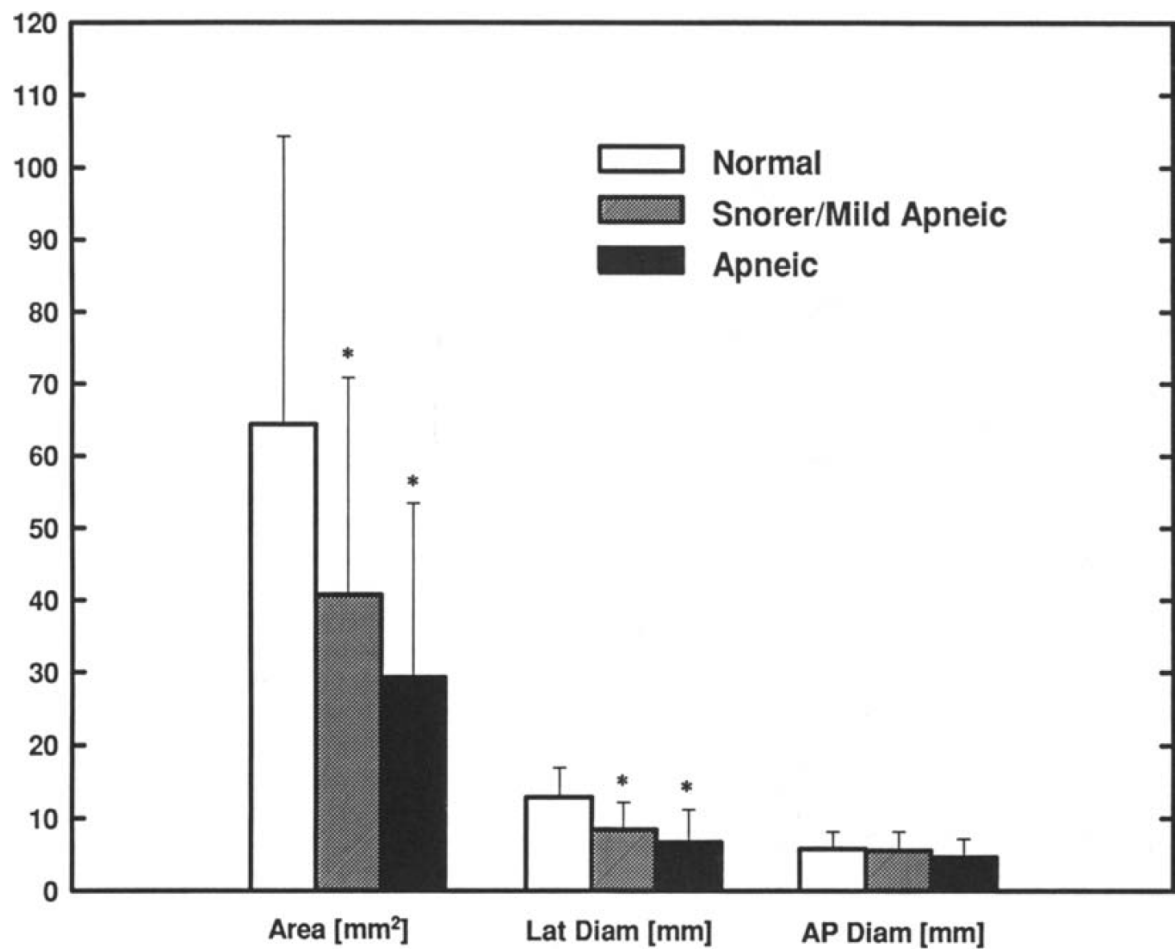


Normal

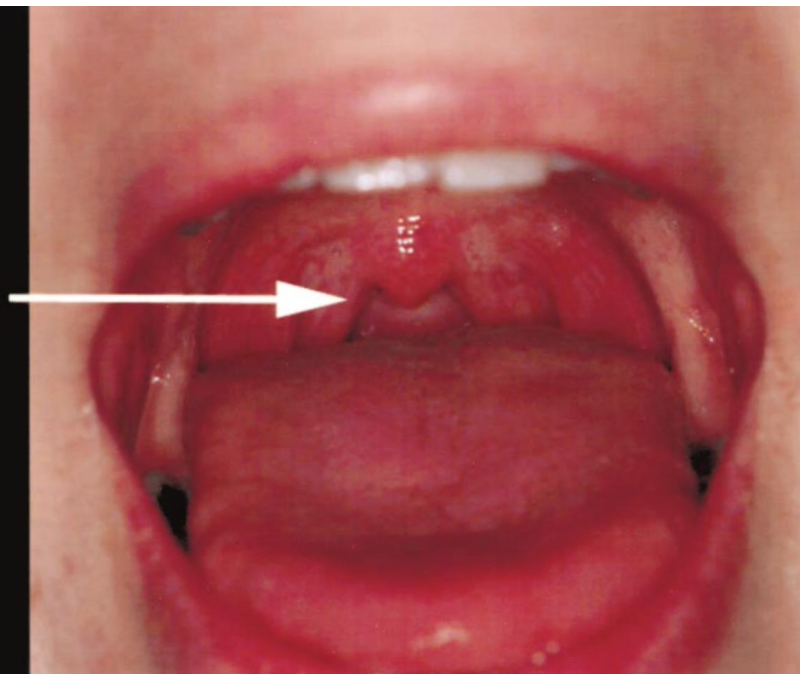


OSA

A **smaller minimum airway area** in patients with OSA in the retropalatal region, and particularly in the **lateral dimension** compared with individuals with normal breathing

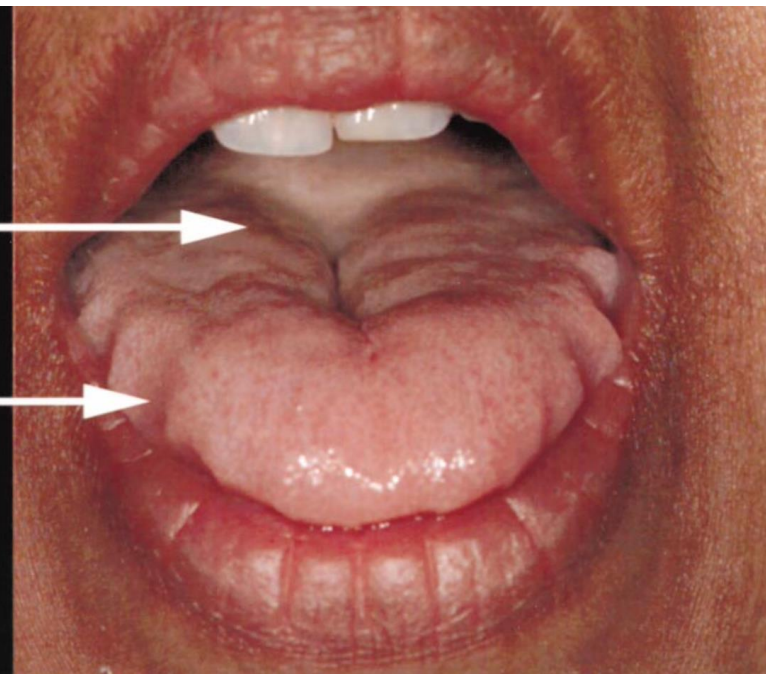


**Lateral
Narrowing**

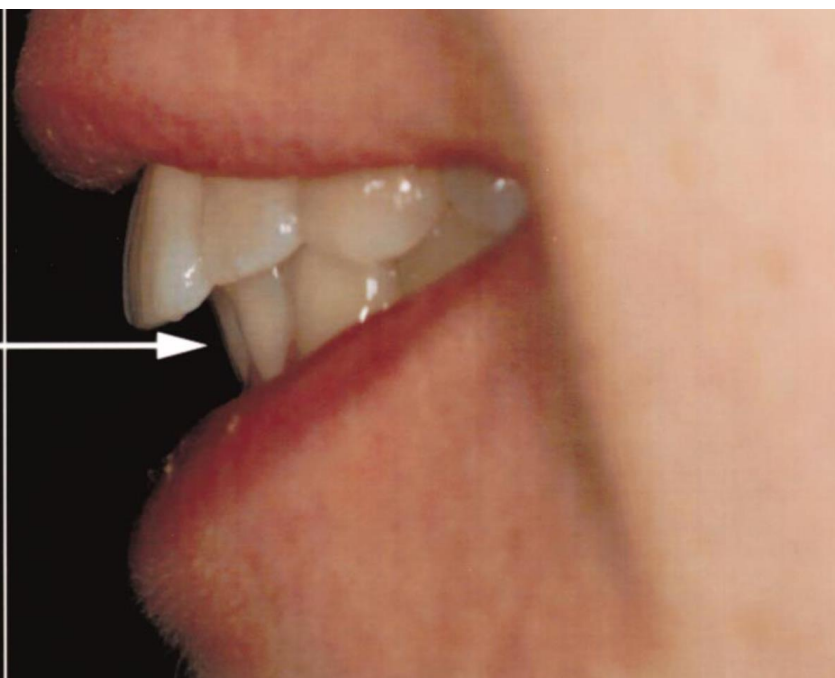


Macroglossia

Tongue ridging



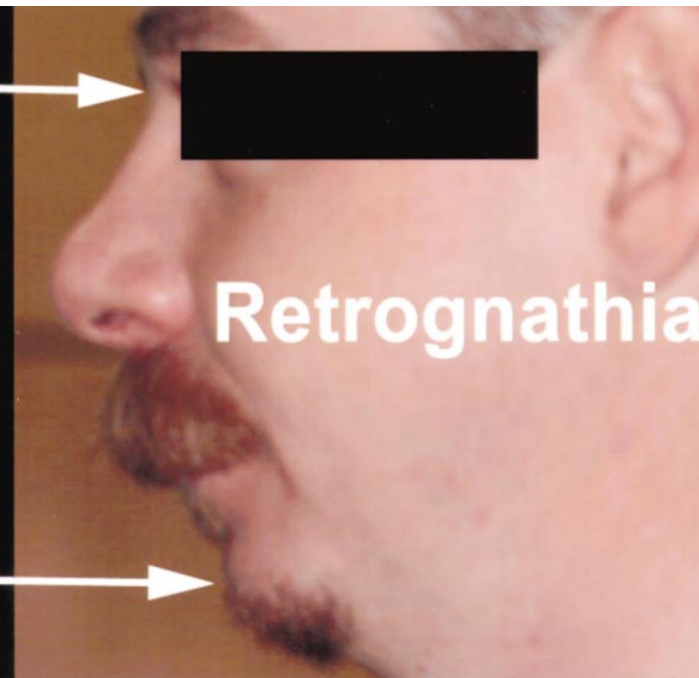
Overjet



Nasion

Retrognathia

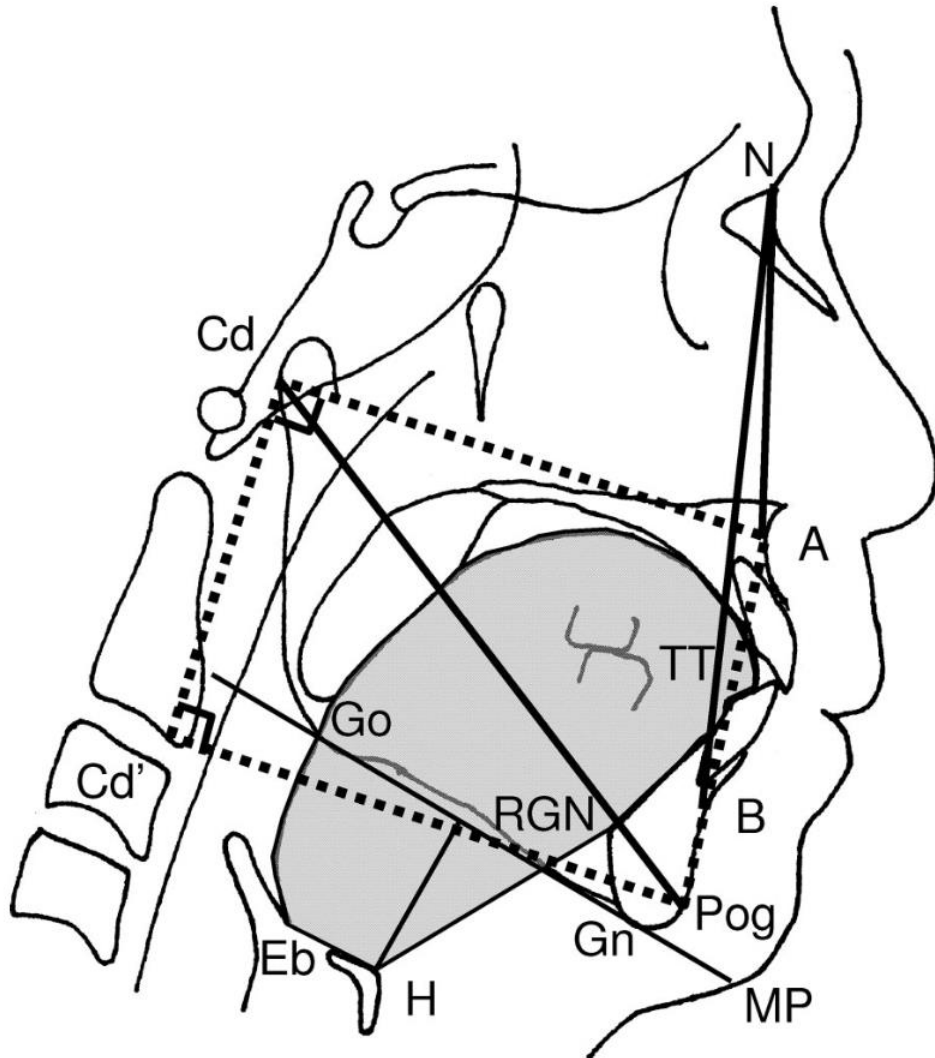
Gnathion



**CRUDE AND ADJUSTED ASSOCIATIONS BETWEEN MORPHOMETRIC
VARIABLES AND OBSTRUCTIVE SLEEP APNEA: MALES***

Structure	n (289 Total)	Percent RDI ≥ 15	Crude OR (95% CI)	Adjusted OR (95% CI)	Backward Regression OR (95% CI)	Backward Regression OR Adjusted for BMI and NC (95% CI)
Lateral narrowing						
Present	157	58.0	4.1	3.3	3.7	2.7
Absent	132	25.0	(2.5–6.9)	(1.9–5.7)	(2.2–6.1)	(1.6–4.8)
Uvula enlarged						
Present	136	54.4	2.5	1.8	2.0	NS
Absent	153	32.7	(1.5–4.0)	(1.1–3.0)	(1.2–3.3)	
Tonsils enlarged						
Present	34	67.7	3.2	2.3	NS	NS
Absent	255	39.6	(1.5–6.8)	(1.0–5.3)		
Tongue enlarged						
Present	228	47.0	2.3	2.4	NS	NS
Absent	61	27.9	(1.2–4.2)	(1.2–4.8)		
Low-lying palate						
Present	179	44.1	1.1	1.1	NS	NS
Absent	110	40.9	(0.7–1.8)	(0.6–1.9)		
Retrognathia						
Present	122	45.1	1.2	1.1	NS	NS
Absent	167	41.3	(0.7–1.9)	(0.6–1.9)		
Overjet						
Present	35	45.7	1.1	1.8	NS	NS
Absent	254	42.5	(0.6–2.3)	(0.6–4.2)		

Anatomical imbalance – tongue size



Dotted lines → lower face cage

Shaded area → tongue cross sectional area

(A) OSA

(B) non-OSA

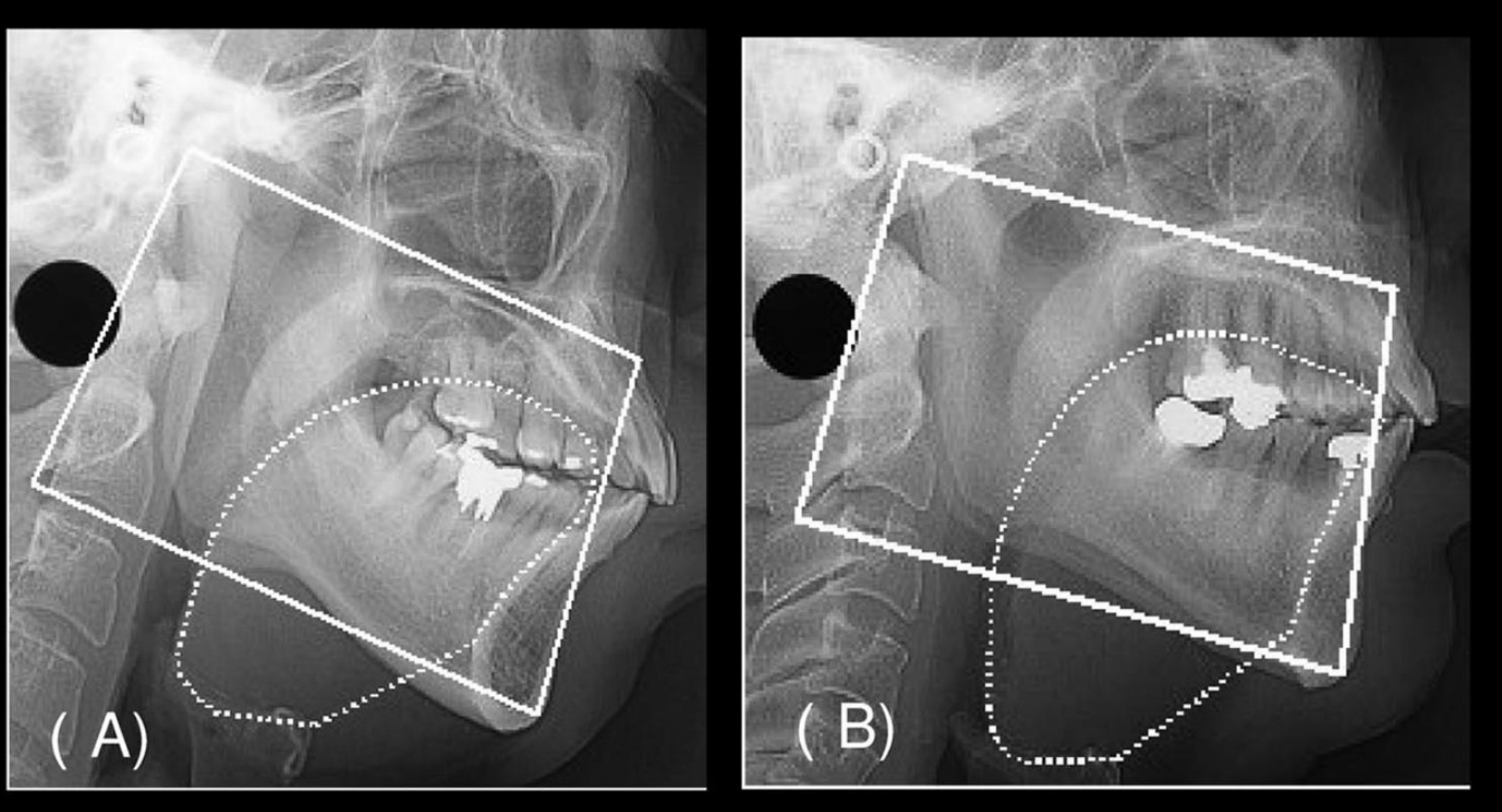
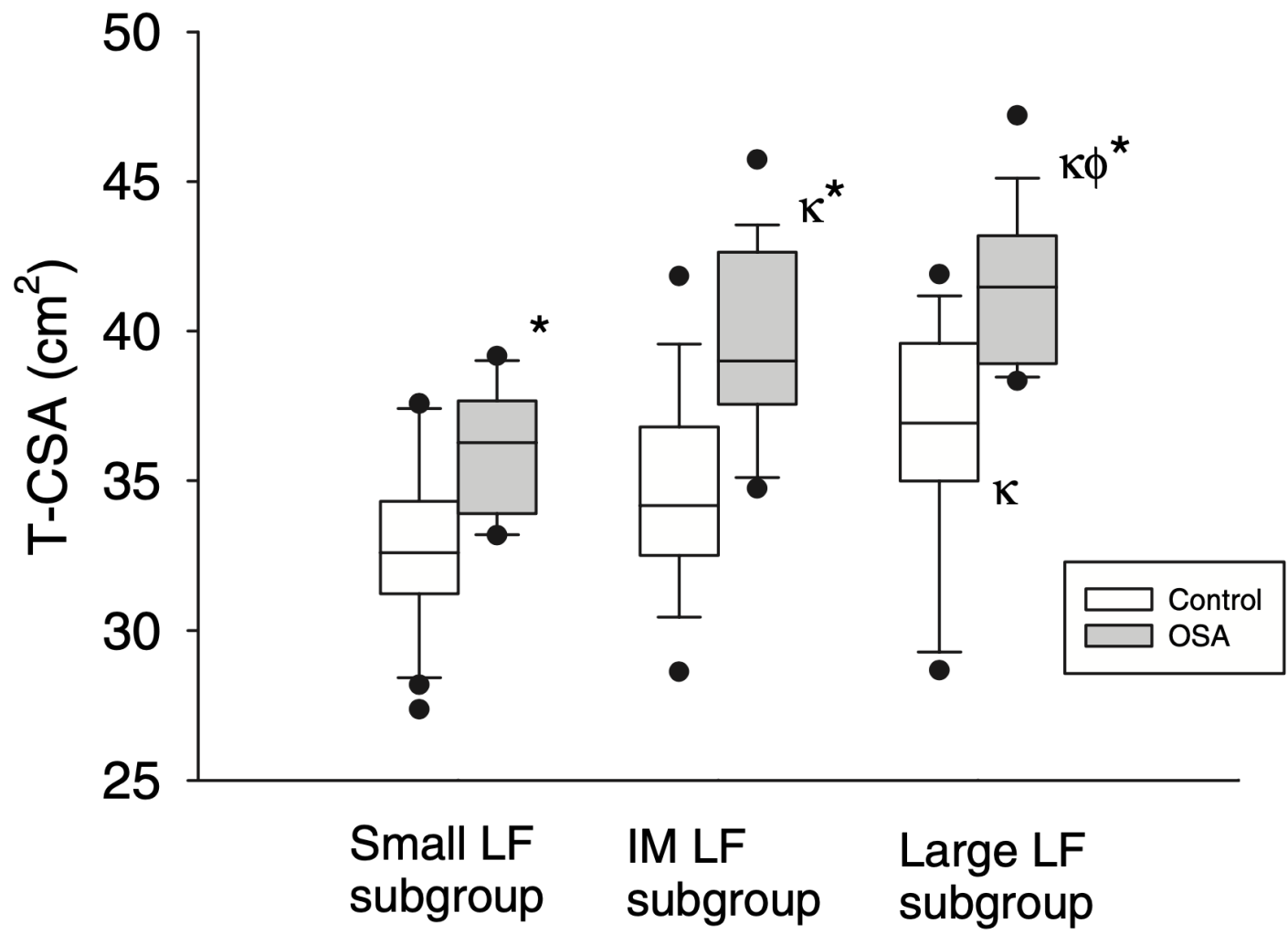


Fig. 2. Representative cephalograms illustrating interaction between craniofacial dimensions and tongue size for obstructive sleep apnea development. The obstructive sleep apnea patient (A) had equivalent size of the lower face cage (78 vs. 77 cm²) but had larger tongue cross-sectional area (41.5 vs. 35.0 cm²) compared with the non-obstructive sleep apnea subject (B).



Relative size of the tongue

Oropharyngeal crowding

TG/LFC = tongue size / lower face cage

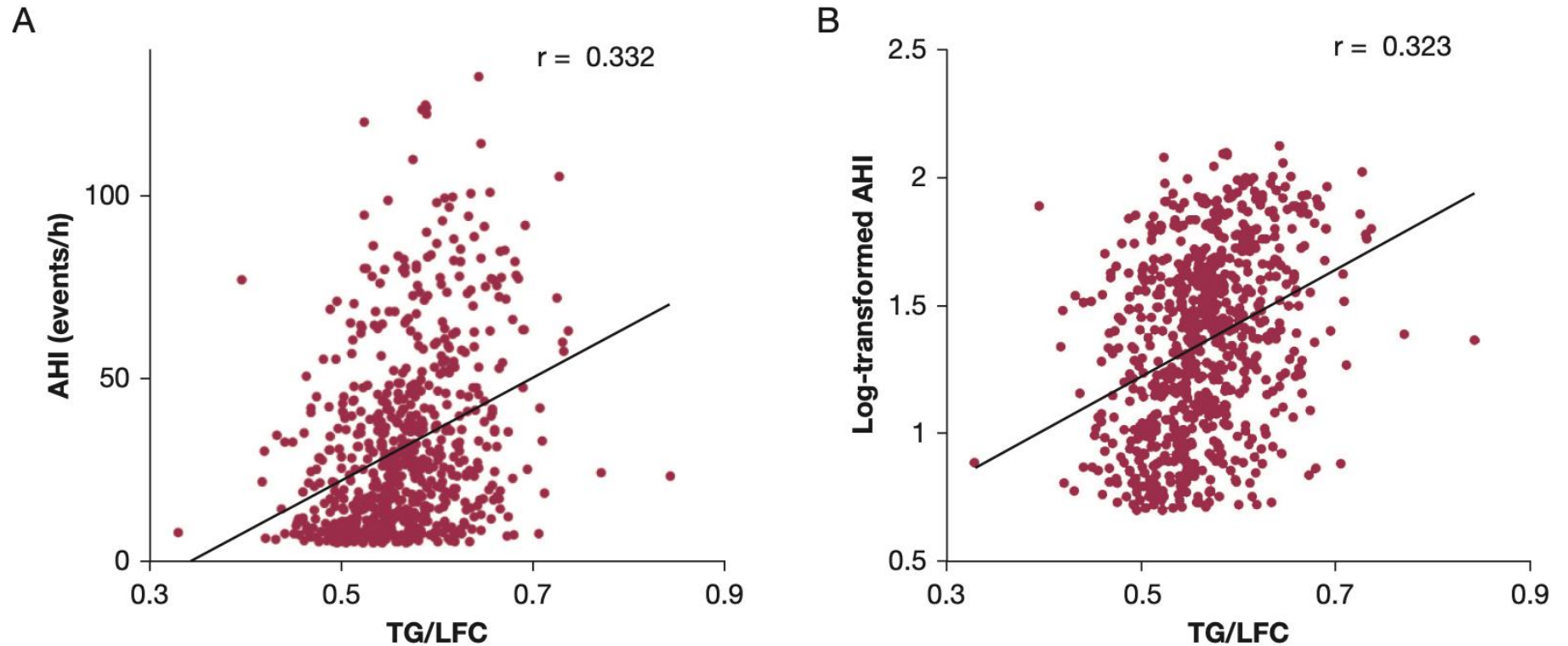
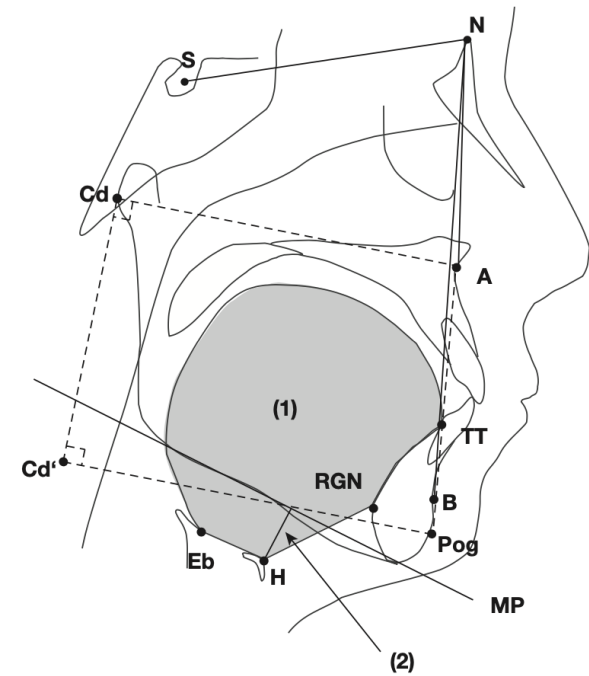
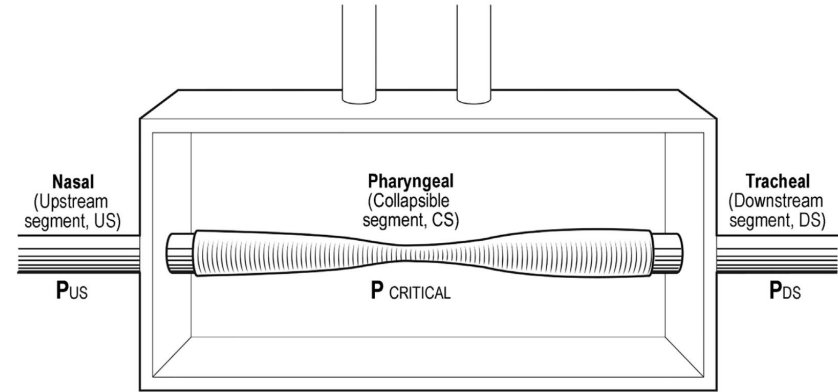
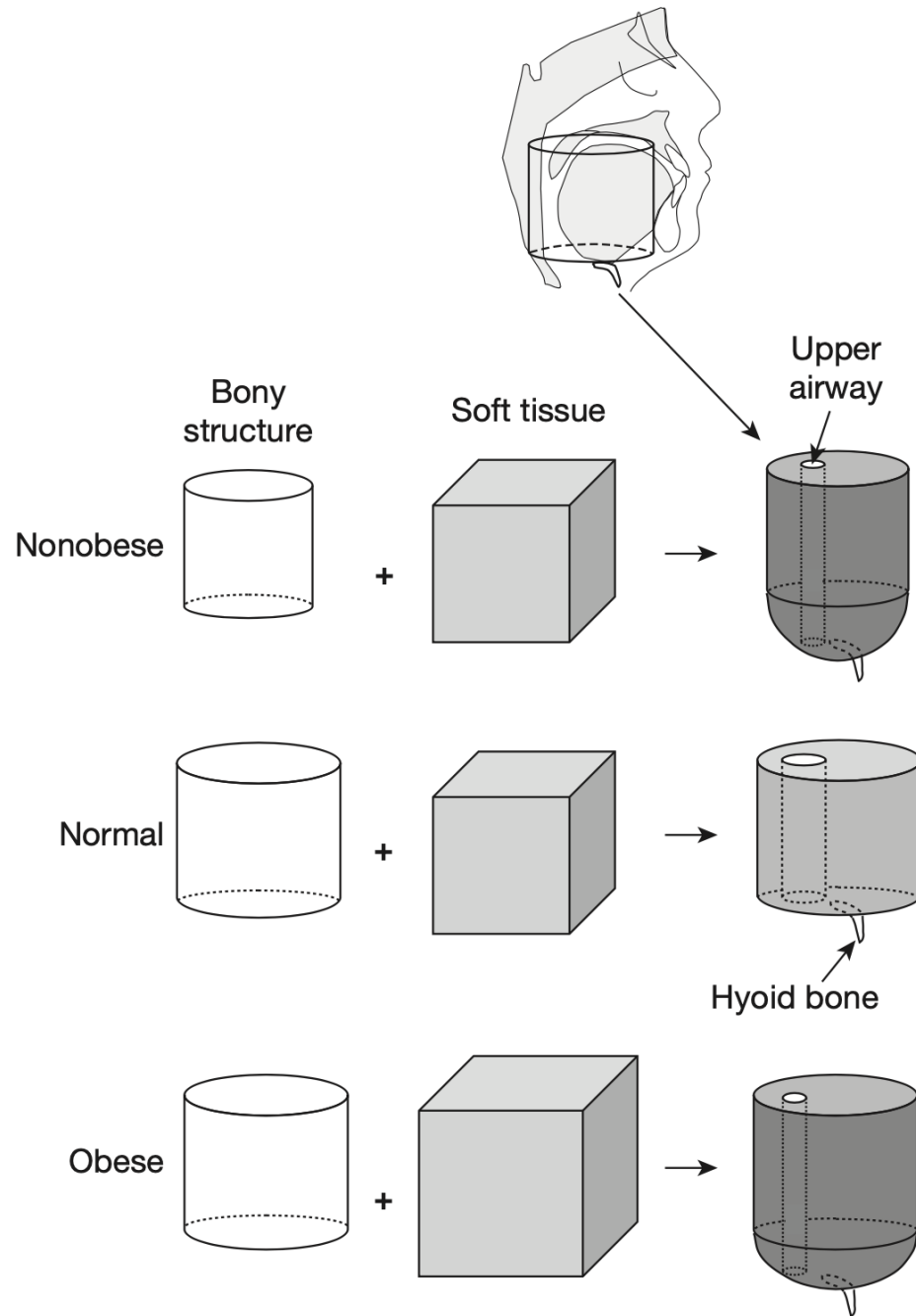


Figure 2 – Relationship between (A) AHI or (B) log-transformed AHI and TG/LFC in 703 OSA subjects. (A) Correlation coefficient = 0.332, $P < .001$, and (B) correlation coefficient = 0.323, $P < .001$ by using Pearson product-moment correlation coefficients. AHI = apnea-hypopnea index; TG/LFC = ratio between the tongue size and lower face cage (ie, degrees of oropharyngeal crowding).

TABLE 3] Stepwise Multiple Linear Regression Analysis With Log-Transformed AHI as the Dependent Variable

Obese (BMI \geq 30 kg/m ² , n = 158)					
R ² (AdR ²)	Predictor	B (95.0% CI)	β (95.0% CI)	t Value	P Value
0.294 (0.285)	(Constant)	-1.249 (-1.960 to -0.539)		-3.474	.001
	TG/LFC	3.130 (2.261-4.000)	0.480 (0.347-0.613)	7.112	< .001
	BMI	0.028 (0.014-0.043)	0.268 (0.134-0.412)	3.972	< .001
Nonobese (BMI < 30 kg/m ² , n = 545)					
R ² (AdR ²)	Predictor	B (95.0% CI)	β (95.0% CI)	t Value	P Value
0.205 (0.200)	(Constant)	-1.723 (-2.252 to -1.195)		-6.407	< .001
	Age	0.019 (0.014-0.024)	0.307 (0.226-0.388)	7.927	< .001
	BMI	0.044 (0.029-0.059)	0.226 (0.149-0.345)	5.628	< .001
	TG/LFC	1.220 (0.429-2.011)	0.123 (0.043-0.203)	3.030	.003
	MP-H	0.009 (0.002-0.016)	0.098 (0.022-0.174)	2.541	.011

AdR² = adjusted R squared; B = unstandardized coefficients; β = standardized coefficients. See [Table 1](#) legend for expansion of other abbreviations.



The luminal size is determined by the properties of the tube and the transmural pressure

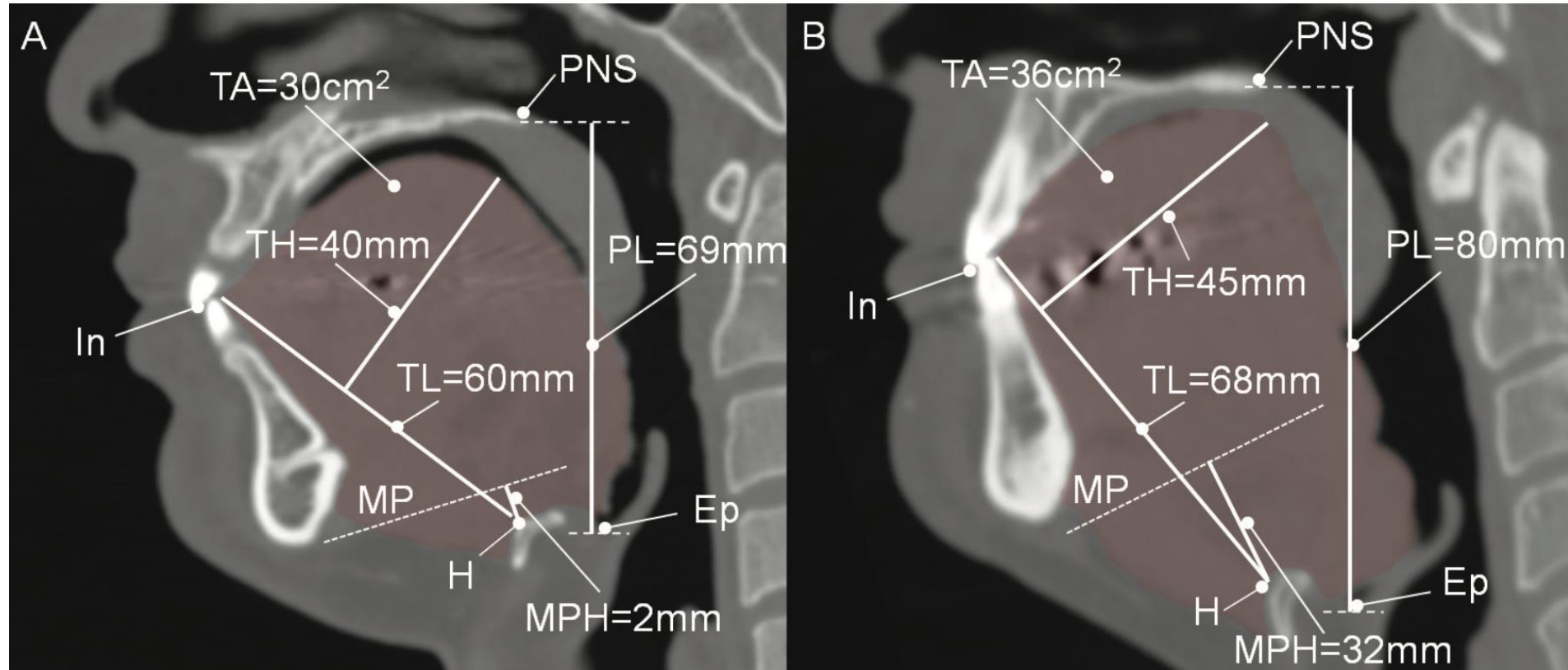
= difference between pressures inside and outside the tube

Increase in the outside tissue pressure
 → luminal narrowing

Upper airway collapsibility

- P_{crit} will increase as tissue pressure increases from a **reduction in size of the bony box**
(micrognathia, a high arched palate, or mid-face hypoplasia)
from **soft tissue crowding**
(macroglossia, adenotonsillar hypertrophy, and central adiposity)
- Obesity acts synergistically with narrowing of the bony box

Inferiorly placed hyoid bone



(A) subject with minimal sleep disordered breathing

(AHI=12, $P_{crit}=-3.1$ cm H₂O, BMI=27 kg/m²)

(B) subject with severe OSA

(AHI=32, $P_{crit}=0.2$ cm H₂O, BMI=29 kg/m²)

Table 1—Anthropometric and upper airway characteristics according to the median of pharyngeal critical closing pressure.

	Whole group (n = 34)	Pcrit ≤ 1.52 (n = 17)	Pcrit ≥ 1.52 (n = 17)
Anthropometric data and OSA severity			
Age, y	47.5 ± 13.5 (22–69)	44.5 ± 15.3	50.5 ± 11.0
BMI, kg/m ²	28.3 ± 3.5 (20.9–38.9)	27.6 ± 3.0	29.0 ± 3.9
Neck circumference, cm	40.9 ± 3.2 (34–48.5)	39.9 ± 3.0	41.9 ± 3.2
Waist circumference, cm	97.4 ± 10.1 (69–124)	95.1 ± 9.7	99.7 ± 10.2
AHI, events/h	29.2 [13.3–50.6] (1.3–90.1)	14.1 [11.4–38.3]	40.4 [29.2–61.5]
Minimum O ₂ sat, %	83.5 [73–87] (60–92.3)	86 [79–90]	78 [64–85]
Upper airway anatomical characteristics			
MPH, mm	14.7 ± 7.9 (2.1–32.1)	10.7 ± 6.3	18.8 ± 7.3
Pharyngeal length, mm	69.7 ± 8.5 (54.7–87.6)	65.5 ± 7.3	73.8 ± 7.6
Tongue length, mm	63.9 [60.1–70.6] (54.9–88.3)	61.0 [57.5–66.1]	68.7 [63.4–74.0]
Tongue height, mm	43.4 ± 3.2	42.4 ± 2.8	44.5 ± 3.2
Tongue volume, cm ³	134.7 ± 16.6 (109.8–174.3)	128.74 ± 13.4	139.3 ± 17.5
Upper airway volume, cm ³	4.8 ± 2.2	4.8 ± 1.9	4.9 ± 2.6

Values in parentheses represent the range of values for the group. Values in solid brackets represent interquartile range for cases in which a variable was not normally distributed. Otherwise standard deviation is quoted. AHI, apnea-hypopnea index; BMI, body mass index; MPH, mandibular plane to hyoid distance; OSA, obstructive sleep apnea; Pcrit, pharyngeal critical closing pressure.

Upper airway dilator muscle activity

- **During wakefulness**

A **higher activity level** in the upper airway dilator muscles in patients with OSA than in normal subjects

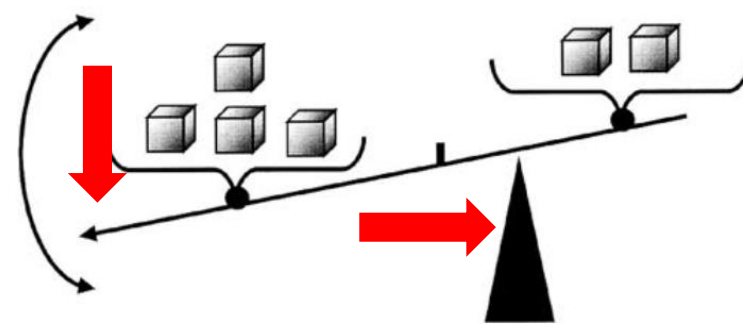
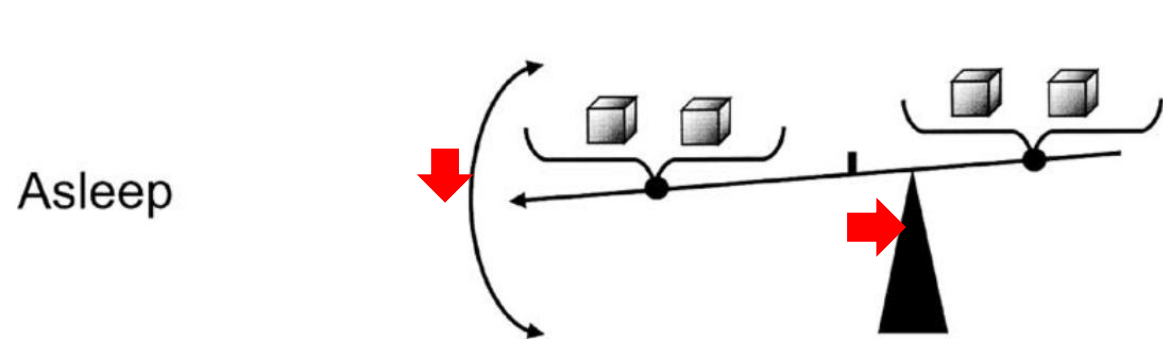
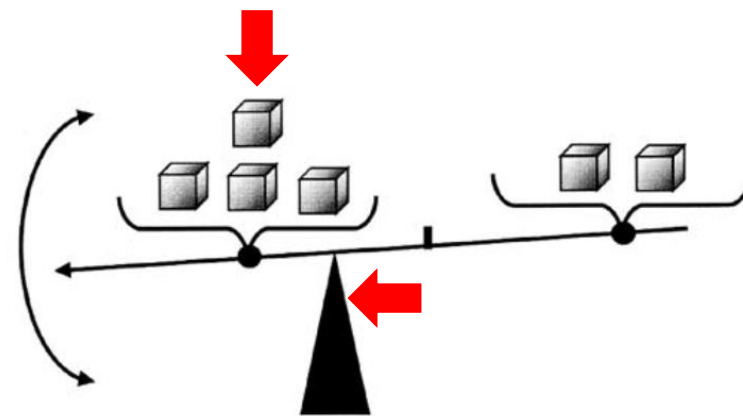
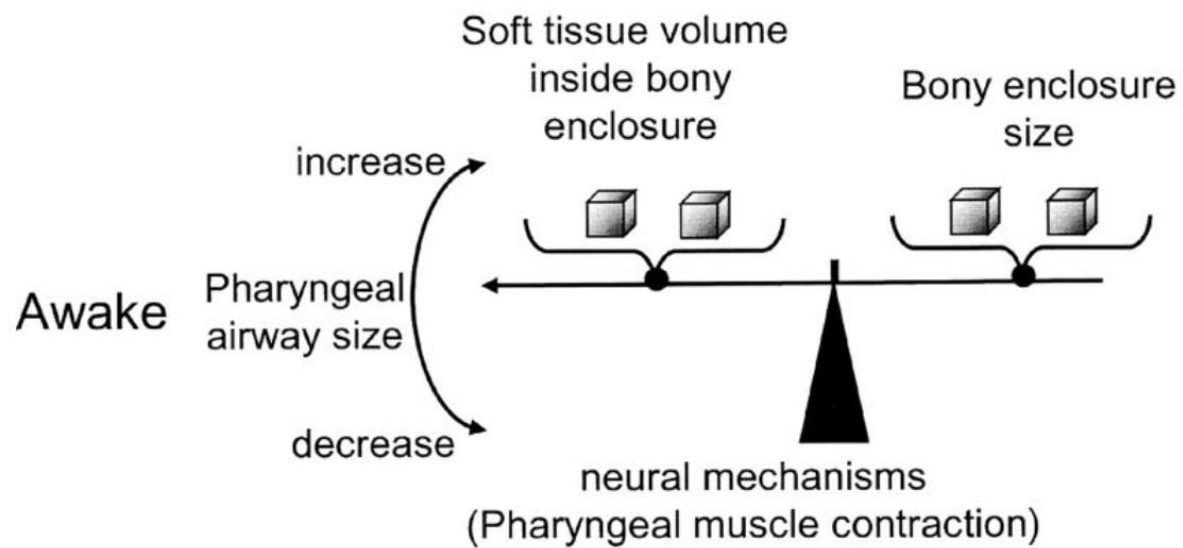
- **Within the onset of sleep**

Reduced upper airway dilator activity both in patients with OSA and in normal subjects

In OSA → compromised and narrow pharyngeal anatomy
+ reduced airway dilator activity leads to airway collapse

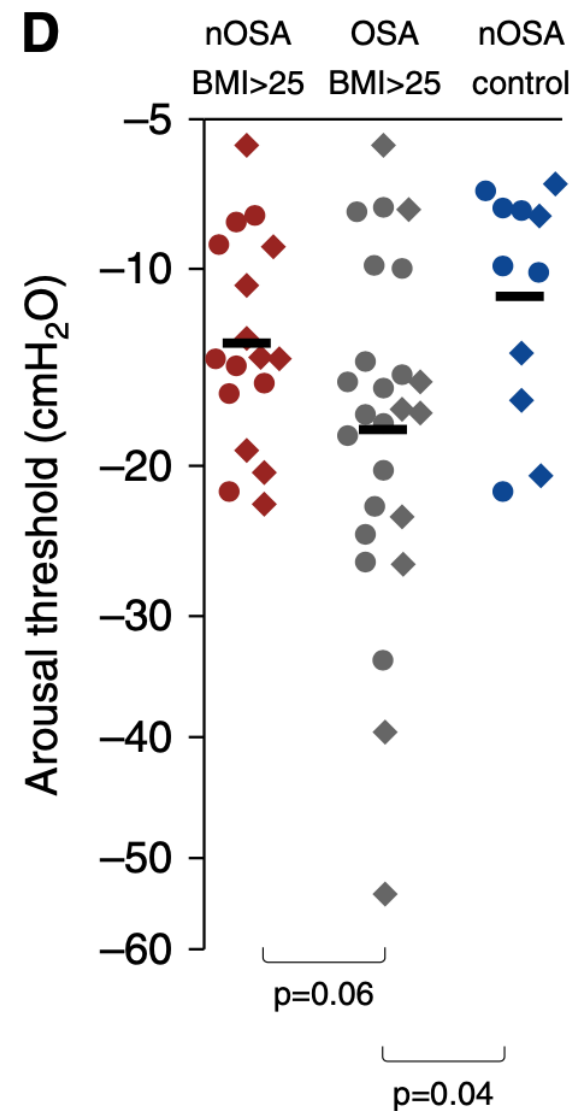
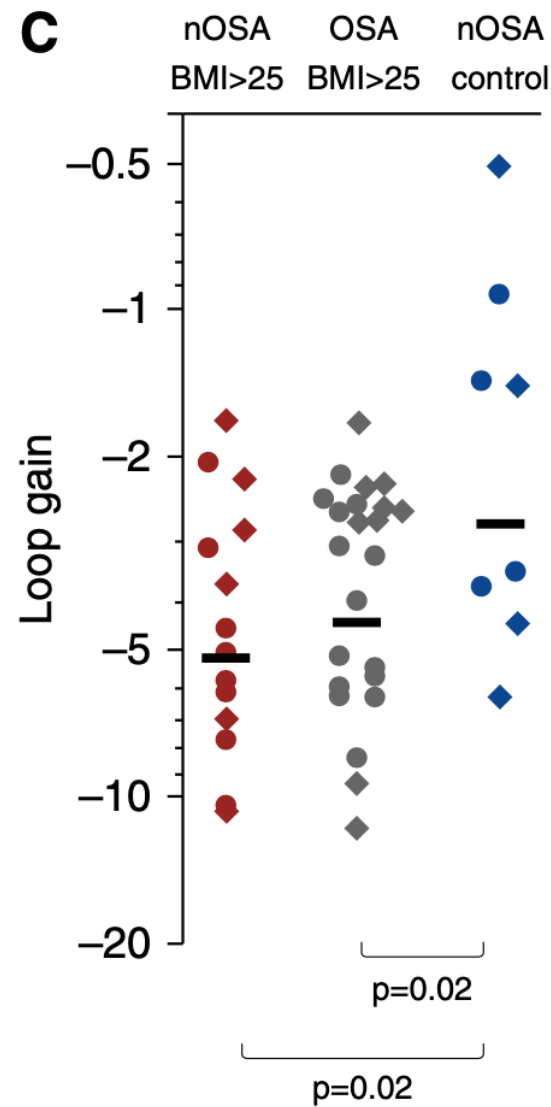
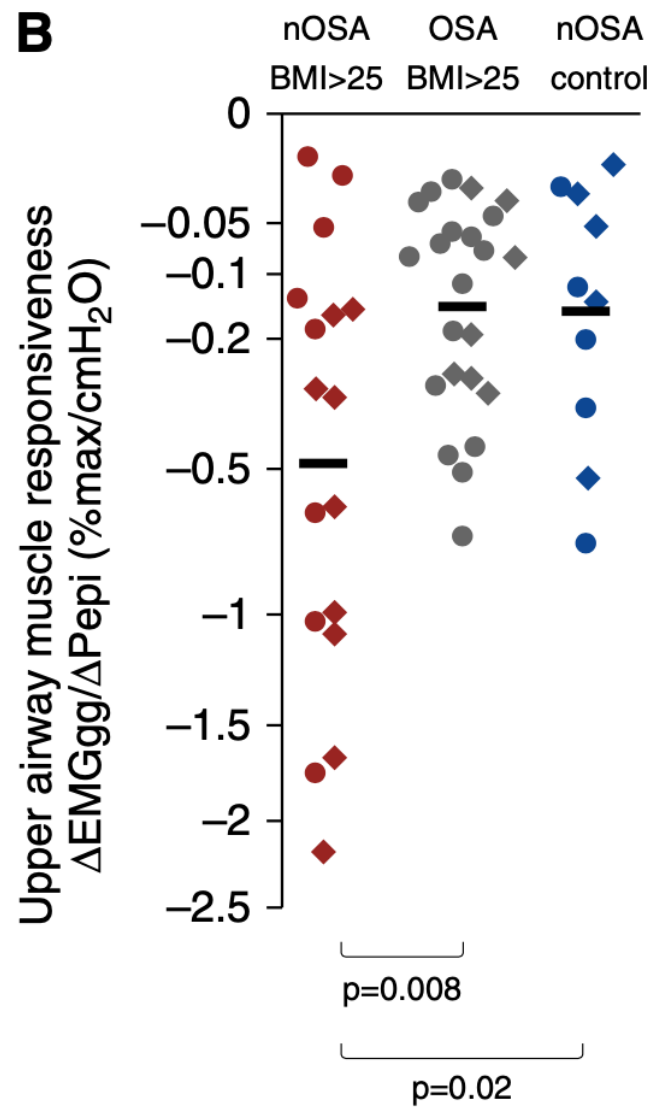
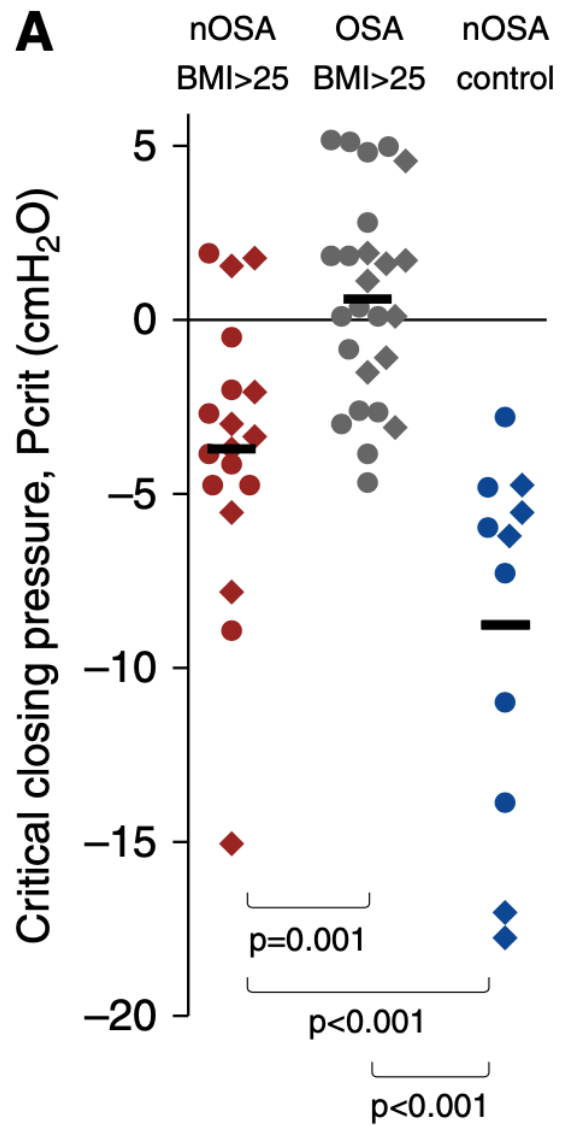
Non-OSA

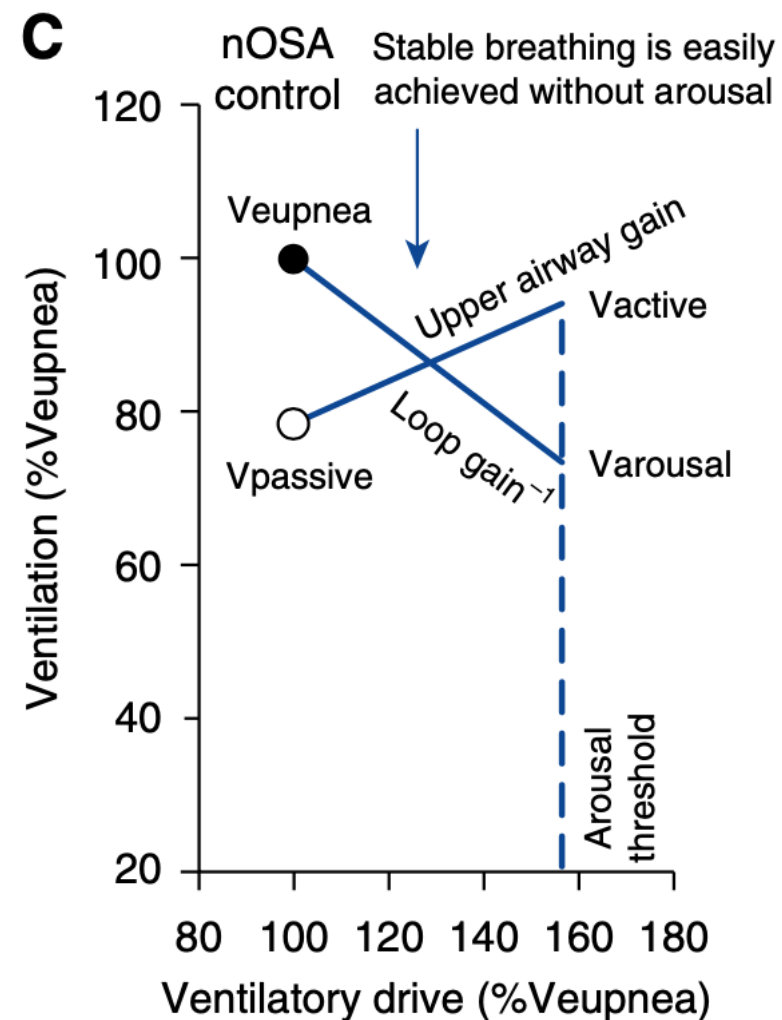
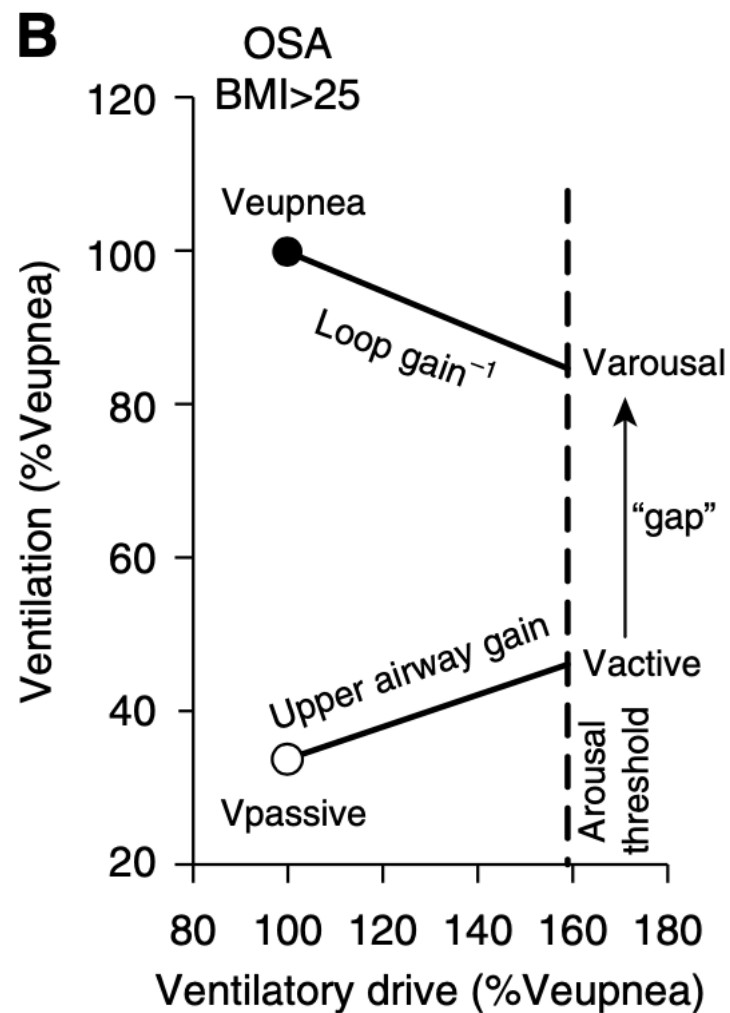
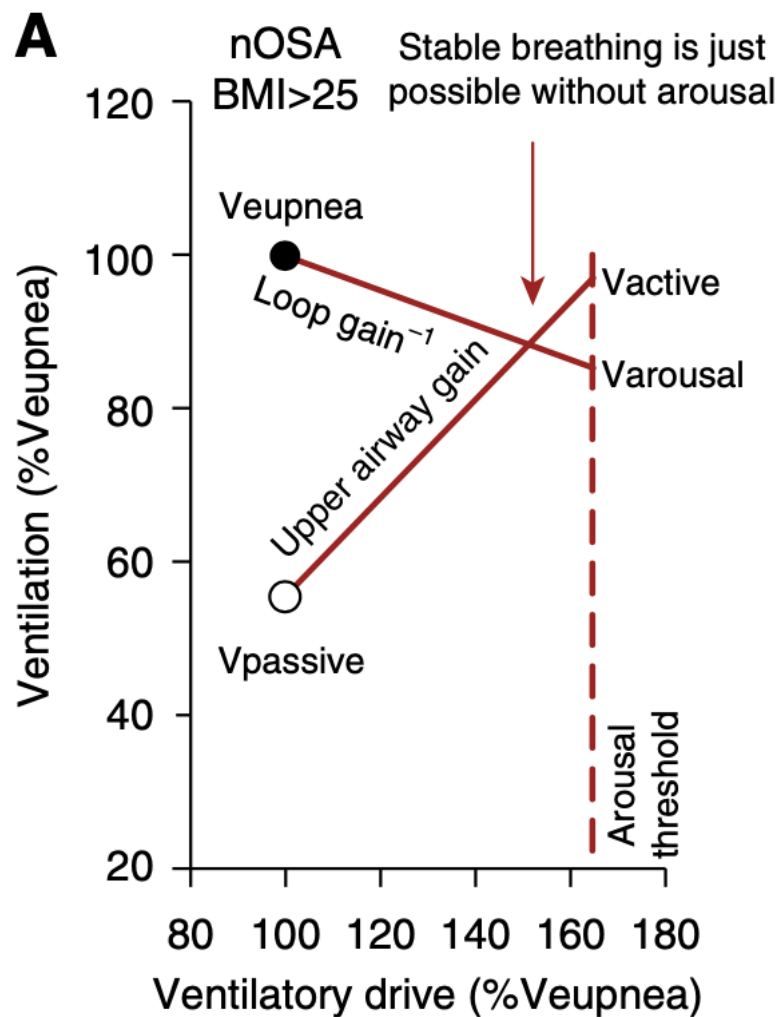
OSA



Enhanced upper airway muscle responsiveness

→ can be protective in certain patients with anatomical impairment





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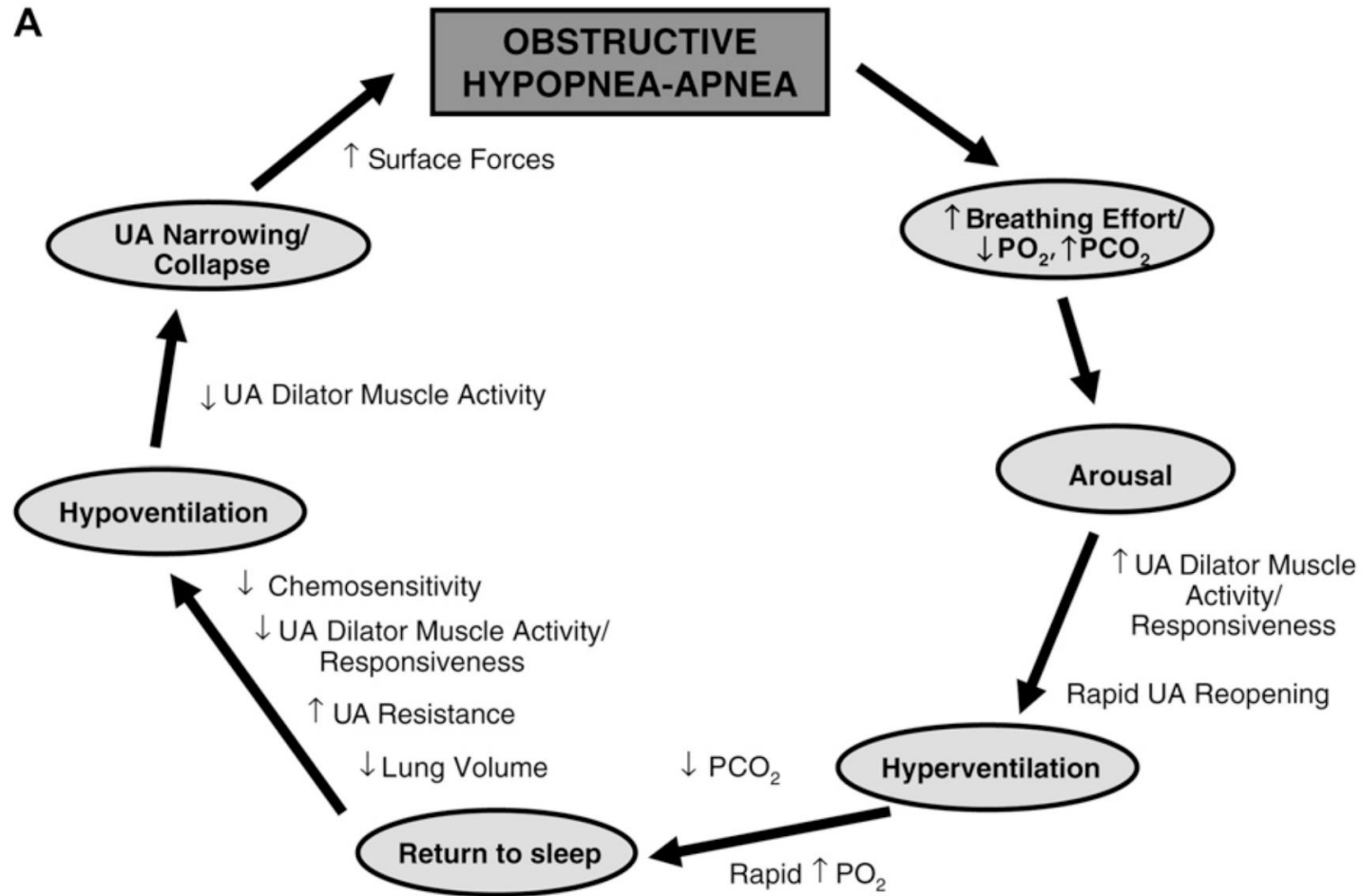
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Ventilatory control instability

Typical feature of OSA: cyclic breathing pattern

Oscillation between obstructive breathing events and arousal

Ventilatory control instability



Ventilatory control instability

Loop gain > 1.0 : respiratory event cycling

Loop gain < 1.0 : stable breathing

High loop gain

→ a ventilatory response to hypopnea that **overcorrects** the changes in blood gas tensions produced by that hypopnea

→ This overcorrection leads to a second hypopnea and the cycle repeats

Ventilatory control instability

- **High loop gain**

- found in systems with large swings in blood gases and ventilation
 - e.g., periodic breathing in congestive heart failure, severe OSA
- approximately 30% of patients with OSA have high loop gain

- **Low loop gain**

- relatively a stable system
- found in a system that may not respond adequately to a reduction in ventilation
 - e.g., obesity hypoventilation

Summary

- Velopharynx and oropharynx are the most collapsible regions in the upper airway
- Several anatomical factors contribute to OSA by inducing airway collapse (e.g., lateral pharyngeal wall thickness, oropharyngeal crowding, etc..)
- Sleep reduces upper airway dilator muscle activity
- High loop gain contributes to ventilatory instability