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Obstructive Sleep Apnea: Pathophysiology and Endotypes

Ana Sanchez-Azofra[1], Atul Malhotra[1], Robert L. Owens[1], and William J. Healy[2]

[1] Division of Pulmonary, Critical Care, and Sleep Medicine, University of California, San Diego, San Diego, California; and [2] Division of Pulmonary, Critical Care, and Sleep Medicine, Medical College of Georgia at Augusta University, Augusta, Georgia

ORCID IDs: 0000-0002-9838-9047 (A.S.-A.); 0000-0002-9509-1827 (A.M.); 0000-0002-6515-6204 (R.L.O.); 0000-0003-4515-5041 (W.J.H.)

WHAT IS OBSTRUCTIVE SLEEP APNEA?

Obstructive sleep apnea (OSA) is a prevalent condition characterized by recurring upper airway collapse during sleep. This can cause reduced breathing (i.e., hypopneas) or complete cessation of breathing (i.e., apneas), which may lead to nocturnal desaturation, hypercapnia, and sleep arousals (Figure 1) (1).

WHAT ARE THE ENDOTYPES OF OBSTRUCTIVE SLEEP APNEA?

The term OSA encompasses a heterogeneous pathology with multiple possible causes. The underlying physiologic mechanisms that lead to the clinical expression of OSA are endotypes. Endotypes can provide valuable guidance in suggesting the best treatment plan for each patient with OSA. Currently accepted endotypes include anatomical compromise of the upper airway, unstable ventilatory control (i.e., increased loop gain), low arousal threshold, and pharyngeal dilator muscle dysfunction. Endotypes can be determined with mathematical analysis of polysomnography data or through direct measurements.

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Correspondence and requests for reprints should be addressed to William J. Healy, M.D., Division of Pulmonary, Critical Care, and Sleep Medicine, Medical College of Georgia, 1120 15th Street, BBR 5513, Augusta, GA 30912. E-mail: wihealy@augusta.edu.

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HOW IS EACH ENDOTYPE DEFINED AND HOW IS IT RELEVANT TO TREATMENT?

Anatomical Compromise

Anatomical compromise refers to the anatomical susceptibility of the upper airway to obstruction, measured as the critical pressure at which the airway collapses (2). Patients with OSA consisting mainly of anatomical compromise may benefit from surgical treatments. Examples include reduced upper airway cross-sectional area and soft tissue arrangement. Anatomical compromise can be addressed with therapies like continuous positive airway pressure therapy and mandibular advancement devices.

Unstable Ventilatory Control

Unstable ventilatory control, also described as loop gain, represents the respiratory system's sensitivity in adjusting breathing in response to changes in CO_2 tension/partial pressure levels. Patients with high loop gain have exuberant responses to fluctuations in partial CO_2 pressure and are more likely to experience failed anatomical interventions to control breathing (3).

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- Obstructive sleep apnea (OSA) consists of recurrent episodes of partial or complete upper airway collapse during sleep, which may lead to gas-exchange abnormalities and arousals from sleep to improve airflow.
- Endotypes are the underlying physiological mechanisms that lead to the clinical expression of OSA.
- The four identified OSA endotypes are anatomical compromise, unstable ventilatory control, low arousal threshold, and impaired pharyngeal dilator muscle function.
- Treatment directed at the physiological causes of a patient's OSA may eventually lead to improved healthcare outcomes.

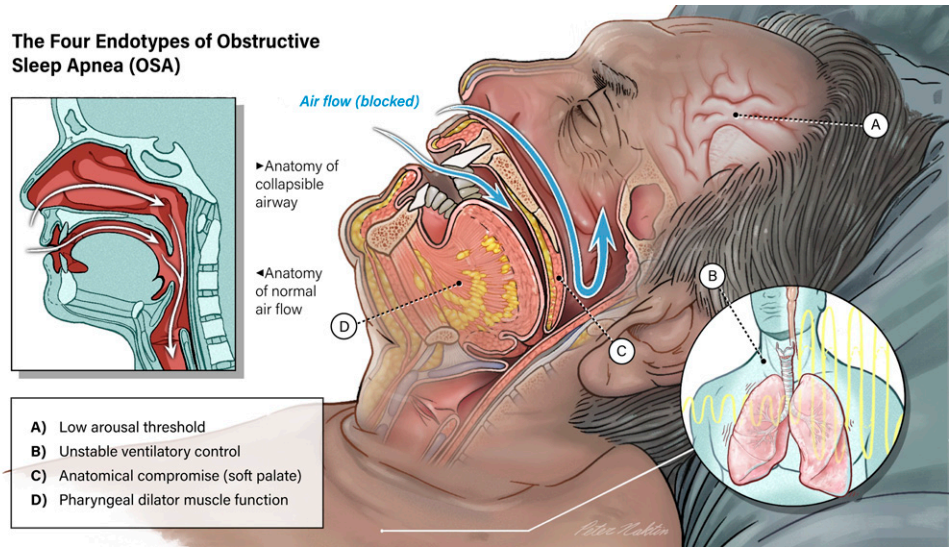

Figure 1. The four currently identified obstructive sleep apnea endotypes. Reprinted by permission from © 2023 Augusta University and Peter Naktin.

Unstable ventilatory control can be targeted through mechanisms to lower the loop gain such as oxygen or acetazolamide.

Low Arousal Threshold

Patients with a low arousal threshold require minimal stimulus to awaken themselves in response to a respiratory event. This situation does not allow sufficient accumulation of signals from respiratory stimuli to activate pharyngeal dilating muscles (4). Patients with a low arousal threshold can be treated with mechanisms to increase the arousal threshold such as hypnotic agents. Approximately one-third of patients present with a low arousal threshold.

Impaired Pharyngeal Muscle Dilator Function

Patients with OSA have increased airway dilator muscle activity while awake compared with those without OSA. These differences may become problematic during sleep, when there is a loss of these reflexes (5). Treatments to improve pharyngeal dilator function such as the use of electrical stimulation devices during sleep or neuromuscular electrical stimulation training during wakefulness are an area of investigation.

CONCLUSIONS

OSA is a composite of the multifactorial physiologic mechanisms, or endotypes, that contribute to its presence and severity. Continued validation and pragmatic implementation in software will be necessary before endotypes are more widely used. Through identification and treatment corresponding with the correct physiological mechanisms, patients can benefit from reduced healthcare costs and more timely interventions, with a reduction in harm associated with inappropriate and ineffective interventions.

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