Sleep and Breathing

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KEYWORDS

• Sleep • Breathing • Respiratory physiology • Sleep-disordered breathing

KEY POINTS

- Complex interaction between neurophysiological controllers and mechanical effectors regulate ventilation.
- Upper-airway narrowing and excess weight along with sleep related positional changes affect the mechanics of breathing and gas exchange.
- These changes are further magnified in certain disease states, such as COPD, restrictive respiratory disorders, neuromuscular conditions, and cardiac diseases.

INTRODUCTION

Control of breathing during sleep involves a complicated physiologic process that differs from that during wakefulness. Complex neurologic and respiratory mechanisms are impacted by host disease states, including specific sleep-related anatomic considerations (eg, upper airway, intercostal, and diaphragm muscles). Derangements in any of these factors can give rise to abnormalities of gas exchange, such as hypoxemia and hypercapnia, or sleep-disordered breathing, including snoring, obstructive and central sleep apneas, Cheyne-Stokes respiration, Biot breathing, and the various hypoventilation syndromes. This article introduces the basic physiology and concepts that are discussed in greater detail in the ensuing articles.

This article discusses the regulation of breathing during sleep as well as screening, diagnostic approaches, and current treatment modalities for sleep-disordered breathing.

NEURAL CONTROL OF BREATHING DURING SLEEP

Medullary respiratory neurons, including the dorsal respiratory group (DRG), ventral respiratory group (VRG), and cranial motor neurons innervating the pharyngeal and laryngeal muscles, receive efferent fibers from the pontine respiratory group.[1] The dorsomedial medulla in the ventrolateral nucleus of the solitary tract contains inspiratory neurons, whereas the VRG contains the nucleus ambiguous, expiratory neurons (Bötzinger complex and caudal retroambigualis), and inspiratory neurons (pre-Bötzinger complex and rostral retroambigualis).[2,3] Pre-Bötzinger complex neurons are thought to possess pacemakerlike properties that generate the basic respiratory rhythm.[4,5]

Afferent neurons (vagal from the lung, carotid/aortic chemoreceptors and baroreceptors) project to the dorsal respiratory group and assorted subnuclei of the medullary solitary tract. Information regarding $Paco_2$, Pao_2, acid-base balance (pH), and blood pressure are integrated via this mechanism. Inspiratory and expiratory neurons are also present in the ventral respiratory group.[2,3] Motor neurons innervating the pharyngeal and laryngeal muscles are located in subregions of the nucleus ambiguus and extend rostrocaudally.[1] Cranial nerves (hypoglossal, trigeminal, and facial motor nuclei) innervate the upper airway muscles to maintain the latter's patency.[6] Finally, the DRG and VRG neurons project to spinal motor neurons that, in turn, innervate their respective respiratory muscles.[2,3]

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The respiratory propriobulbar, premotor neuron and motor neurons are responsible for generating the respiratory rhythm and the central respiratory drive. There are several models regarding the generation of the respiratory rhythm, namely, the pacemaker, network, and hybrid models.[1,2,5] During inspiration, central neurons (DRG and VRG) innervate the phrenic and intercostal motor neurons. Expiratory neurons inhibit the inspiratory neurons allowing exhalation to occur.[2]

Mechanisms that control the activity of the pharyngeal motor neurons differ from those that control the spinal respiratory muscles.[2] Inspiratory drive to the hypoglossal motoneurons arises predominately from the reticular formation, which provides tonic drive to the respiratory system; it is significantly affected during sleep.[1,2] Activity of muscles with respiratory and nonrespiratory (postural/behavioral) functions, such as intercostal and pharyngeal muscles, is suppressed during sleep.[7]

RESPIRATORY PHYSIOLOGY DURING SLEEP

Muscles of respiration do not possess an intrinsic pacemaker and have to be controlled centrally. The respiratory center responds to chemical information (Pa_{O_2} and Pa_{CO_2}) via the carotid/aortic chemoreceptors and baroreceptors; mechanical information from vagal afferent neurons (stretch, deflation, congestion of lungs); and behavioral data (wakefulness stimulus).[8]

HYPOXIA

Ventilatory response to hypoxia is blunted during sleep.[9–12] A sex difference in hypoxic drive has been described. Hypoxic ventilatory response during wakefulness is much higher in men than women.[12] In addition, although hypoxic ventilatory response is lower during non–rapid eye movement (NREM) sleep than wakefulness among men, it is similar during NREM sleep and waking in women.[9,10] Whether this contributes to the decreased prevalence of sleep-disordered breathing among premenopausal women is unclear.[11–14] The hypoxic ventilatory response declines further during REM sleep.[9–12] Isocapnic hypoxia is not a major stimulus for arousal in normal adults, who can remain asleep even if arterial saturation decreases to as low as 70%.[9–11]

HYPERCAPNIA

The hypercapnic ventilatory response is also reduced during sleep and is most blunted during REM sleep.[15] As in the case with hypoxia, the ventilatory drive to hypercapnia does not change significantly from wakefulness to NREM sleep in women, who have higher ventilatory responses during sleep compared with men.[16,17]

Hypercapnia produces arousals from sleep, generally when end-tidal carbon dioxide levels reach 15 mm Hg more than baseline values.[11,15,18,19] Concurrent hypoxia increases the sensitivity to hypercapnic arousal.[20]

AIRWAY RESISTANCE

Increases in airway resistance, including the addition of inspiratory resistance or occlusion during inspiration, also lead to arousals.[21,22] Arousal frequency increases during NREM stages 2 and 3 sleep and REM sleep when inspiratory resistance is added.[23] The frequency of arousals from additional inspiratory resistance is lowest during slow wave sleep.[24,25] In contrast, airway occlusion produces more arousals during REM sleep.[26,27]

Upper airway resistance is increased during sleep, as a reduction in upper airway muscle tone causes anatomic structures to become more prone to collapse. This effect is compounded by positional changes during sleep or increased vascular congestion.

Regularity of Breathing During Sleep

Irregular breathing patterns can develop during sleep, especially during stages NREM 1 and 2 sleep. Periodic breathing, including episodic central apneas, can arise when carbon dioxide sensitivity and threshold changes from wakefulness (lower) to sleep (higher) levels.[19,28] Experimental hypocapnia with and without hypoxia has been demonstrated to induce irregular breathing patterns during NREM sleep.[29] The apnea threshold is higher in premenopausal women than in both men and postmenopausal women.[30] Hypocapnia in conjunction with increased airway resistance may lead to occlusive apneas.[31]

Respiratory Muscle Function During Sleep

Respiratory functional residual capacity is reduced in the supine, compared with the upright, position because of the relative inability of chest wall expansion to counter an increased abdominal pressure. During REM, sleep-associated atonia of the intercostal muscles results in decreased chest wall compliance and leaves the diaphragm as the sole musculature of respiration. Respiratory muscle atonia along with decreased hypercapnic and hypoxic chemosensitivity, can lead to hypoventilation during REM sleep.

Other important changes in respiratory physiology occur during sleep: (1) reduced ventilatory response to elastic loading, (2) decreased minute