Sleep and Respiratory Physiology in Adults

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KEYWORDS

• Respiratory physiology • Control of breathing • Sleep effects • Hypoventilation • Upper airway • Lower airway

KEY POINTS

- Sleep is a potentially vulnerable state for the respiratory system.
- Respiratory drive is determined by a central respiratory generator located within the brainstem.
- Withdrawal of wakefulness stimuli and the initiation of active sleep processes results in ventilation being determined primarily by metabolic demand.
- The respiratory system is regulated by central and peripheral chemoreceptors and mechanoreceptors that provide negative feedback to maintain ventilation.
- Sleep onset results in alterations in upper and lower airway physiology to maintain eucapnia.

The respiratory system is a complex interplay between the central nervous system, respiratory-related motor neurons, and the muscles of respiration. During wakefulness, both volitional and metabolic pathways are active in determining the minute ventilation necessary to maintain eucapnia (the CO_2 level during stable breathing). With sleep onset, wakefulness stimuli are withdrawn as active central processes for sleep are initiated, leaving metabolic demand as the primary determinant of minute ventilation. Individuals with respiratory abnormalities such as an anatomically small upper airway, restrictive lung disease, obstructive lung disease, or neuromuscular weakness, may depend on the wakefulness stimuli through recruitment of accessory muscles to maintain ventilation. Sleep onset results in a marked reduction of compensatory mechanisms, which can promote hypoventilation and the development of sleep-related breathing disorders. Thus, sleep represents a potentially vulnerable state for the respiratory system.

BASIC RESPIRATORY NEUROBIOLOGY

Respiratory Anatomy and Neuromotor Control

From classical transection experiments, the medulla and pons have been identified as the primary central nervous system location responsible for determining respiratory drive.[1] Medullary respiratory neurons vital to breathing include 2 groups of neurons referred to as the dorsal respiratory group (DRG) and the ventral respiratory group (VRG; **Fig. 1**).[2] The DRG contains predominantly inspiratory neurons and is located in the nucleus tractus solatarius, an area responsible for central sensory integration of vagal afferents coming from the lungs, central chemoreceptors (pH),

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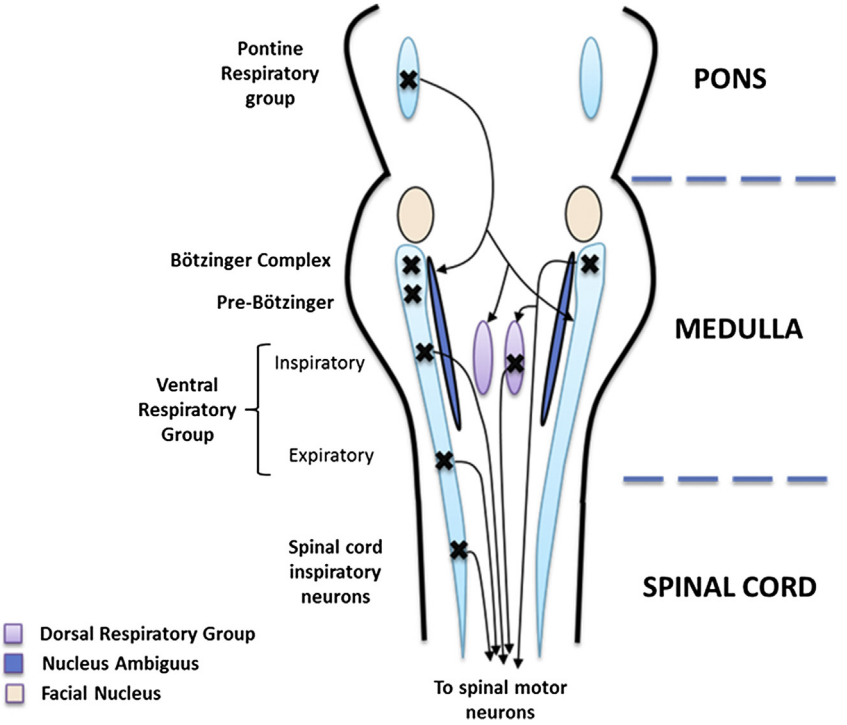

Fig. 1. Brainstem centers contributing to the control of respiratory drive. (*Adapted from* Horner RL. Sleep Research Society basics of sleep guide: control of ventilation. In: Amlaner CJ, Buxton O, editors. Sleep and respiratory physiology in adults. Darien (IL): Sleep Research Society; 2008; with permission.)

carotid and aortic chemoreceptors (CO_2 and O_2), and baroreceptors (blood pressure). The VRG contains both inspiratory and expiratory neurons and includes several important nuclei, or neuronal groups, including the nucleus ambiguus, the Botzinger complex (expiratory neurons), the pre-Botzinger complex (inspiratory neurons), the rostral retroambigualis neurons (inspiratory neurons), and the caudal retroambigualis neurons (expiratory neurons).[2] Bulbospinal neurons from the VRG and DRG then project to spinal motor neurons that innervate the respiratory pump muscles. In close proximity to the VRG are important cranial motor neurons (nucleus ambiguous, contributes to the glossopharyngeal nerve; trigeminal, facial, and hypoglossal nuclei) that innervate muscles of the larynx and pharynx, but are driven by different premotor neurons than those that drive the pump muscles, presumably because the laryngeal and pharyngeal muscles contribute to other functions, such as swallowing and phonation. Above the VRG, in close proximity to the Botzinger complex, is the pre-Botzinger complex, which has pacemakerlike properties that generate an underlying respiratory rhythm.[3] This complex of neurons contains mu-opioid receptors and neurokinin receptors, which has important clinical implications. The mu-opioid receptors when stimulated slow the pacemaker, whereas the neurokinin receptors speed the pacemaker.[4] Neuroactive medications, such as opiates, used in the treatment of pain can, therefore, significantly impact ventilation. The pons also plays an important role in modulating respiratory activity, receiving input from the pontine respiratory group (Kolliker fuse and parabrachial nuclei).[5]

The connections and interactions between respiratory propriobulbar neurons, premotor neurons, and motor neurons, referred to as a central respiratory generator (CRG), are ultimately responsible for producing an underlying respiratory drive (tonic activity) and respiratory rhythm (phasic activity) to the respiratory pump muscles (**Fig. 2**).[2] The level of tonic drive generated by the CRG is based on input from peripheral and central chemoreceptors.[6] During inspiration, the CRG generates phasic activity, through inspiratory premotor neurons from the VRG and DRG that synapse with phrenic and intercostal motor neurons. Inspiratory activity is terminated by inhibitory projections from expiratory neurons in the Botzinger complex to the brainstem and spinal cord. In contrast with the phrenic and intercostal motor neurons, control of respiratory drive to pharyngeal muscle motor neurons, such as the hypoglossal nerve, is not actively inhibited with expiration. Instead, tonic activity to