work of breathing) likely arises from signals transmitted from the motor cortex to the sensory cortex when outgoing motor commands are sent to the respiratory muscles. Motor output from the brain stem may also be accompanied by signals transmitted to the sensory cortex and contribute to the sensation of work of breathing. The sensation of air hunger likely derives from stimuli that increase the drive to breathe (e.g., hypoxemia, hypercapnia, acidemia; mediated by signals from central and peripheral chemoreceptors), as well as airway and interstitial inflammation (mediated by pulmonary afferent signals) and pulmonary vascular receptors. Dyspnea arises, in part, from a perceived mismatch between the outgoing efferent messages to the respiratory muscles and incoming afferent signals from the lungs and chest wall. Chest tightness, often associated with bronchospasm, is largely mediated by simulation of vagal-irritant receptors. Afferent signals from airway, lung, and chest wall mechanoreceptors most likely pass through the brain stem before being transmitted to the sensory cortex, although it is possible that some afferent information bypasses the brain stem and goes directly to the sensory cortex. *(Adapted from RM Schwartzstein: Approach to the patient with dyspnea. In: UpToDate, TW Post (Ed), UpToDate, Waltham, MA. (Accessed on 7 December 2021) 2018 UpToDate, Inc. For more information visit www.uptodate.com.)*

Afferent signals trigger the CNS (brainstem and/or cortex) and include primarily: (1) peripheral chemoreceptors in the carotid body and aortic arch and central chemoreceptors in the medulla that are activated by hypoxemia, hypercapnia, or acidemia, and might produce a sense of “air hunger”; and (2) mechanoreceptors in the upper airways, lungs (including stretch receptors, irritant receptors, and J receptors), and chest wall (including muscle spindles as stretch receptors and tendon organs that monitor force generation) that are activated in the setting of an increased work load from a disease state producing an increase in airway resistance that may be associated with symptoms of chest tightness (e.g., asthma or COPD) or decreased lung or chest wall compliance (e.g., pulmonary fibrosis). Other afferent signals that trigger dyspnea within the respiratory system can arise from pulmonary vascular receptor responses to changes in pulmonary artery pressure and skeletal muscle (termed metaboreceptors) that are believed to sense changes in the biochemical environment.

Efferent signals are sent from the CNS (motor cortex and brainstem) to the respiratory muscles and are also transmitted by corollary discharge to the sensory cortex; they are believed to