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Review

Effects of loading on upper airway and respiratory pump muscle motoneurons

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ABSTRACT

The functional outcomes of respiratory muscle loading by chemical (e.g. hypercapnia), mechanical (i.e. external mechanical loading) or ventilatory (e.g. exercise) factors can be either positive, such as through an increase in pressure-generating capacity of the inspiratory muscles or detrimental, such as by fatigue. Neurophysiological responses to respiratory muscle loading can occur at one or more points along the pathway from motor cortex to muscle. This paper describes the respiratory pump and upper airway motoneuron responses to the imposition of acute loads including processes of pre-activation, respiratory reflexes, potentiation and fatigue. It also considers changes suggestive of adaptation to chronic loading either from specific respiratory muscle training programs or as part of disease processes such as chronic obstructive pulmonary disease or obstructive sleep apnoea.

1. Introduction

The primary purpose of the respiratory muscles is to generate adequate alveolar ventilation to maintain homeostasis of arterial blood gases. The muscles involved include both those of the respiratory pump, which shift air in and out of the respiratory tree, and those of the upper airway, which stabilise the airway to maintain its patency during ventilation and partition flow through the oral and nasal routes. Effective ventilation requires coordinated contraction and relaxation of these muscles and therefore the respiratory muscles require a complex system of neural control. They must contract rhythmically throughout life to ensure adequate ventilation during both sleep and wakefulness, but are also required to participate in other motor tasks including locomotion, postural control, swallowing and speech (Aleksandrov, 2009). Thus the respiratory muscles are under both automatic and volitional control.

Automatic control of breathing in mammals consists of central pattern generators with components located in at least two distinct regions: the pre-Botzinger complex and the parafacial respiratory group (Smith et al., 2009). These pathways are responsible for life-long rhythmic motor output to the upper airway and respiratory muscles. Volitional control originates from multiple areas including the primary motor cortex, supplementary motor area and basal ganglia with widespread input from the cerebellum (Aleksandrov, 2009; Isaev et al., 2002; Sharshar et al., 2004) and descends via the corticospinal pathways. These pathways allow control of the respiratory muscles during activities such as speech and swallowing. Integration of suprabulbar and peripheral inputs is believed to occur at multiple levels including convergence at the level of the cranial or spinal motoneuron pool itself (Butler, 2007) and/or within the premotor projections that synapse onto motoneurons of the upper airway and respiratory pump.

To ensure adequate ventilation, the respiratory pump muscles are required to overcome intrinsic mechanical loads, which are resistive, elastic and threshold in nature (Banner et al., 1994). Resistive loads arise as a result of airflow through the airways and increase when airways are narrowed. Elastic loads reflect those associated with stiffness of the lungs and chest wall and increase when inspiration is performed at higher lung volumes. Threshold loads occur as a consequence of incomplete expiration with the resultant positive intra-alveolar pressure leading to inward recoil of the chest wall and lungs. Threshold loads increase with dynamic pulmonary hyperinflation, particularly in conditions characterised by expiratory airflow limitation, such as chronic obstructive pulmonary disease (COPD) (O'Donnell et al., 2001). In addition to intrinsic loads, additional load can be placed on the respiratory muscles by chemical stimuli (e.g. hypercapnia), mechanical devices (i.e. external mechanical loading) or metabolic factors (e.g. exercise). Loading the respiratory pump or upper airway muscles can have effects which can be considered negative or positive in terms of functional status.

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Impaired performance of the respiratory pump and upper airway muscles is a common feature of respiratory and neuromuscular disease and results in a chronic imbalance between the intrinsic load borne by these muscles and their capacity to maintain adequate ventilation and/or airway patency. This imbalance has important negative functional consequences. For example, in people with cardiorespiratory disorders, reduced pressure-generating capacity of the inspiratory muscles (i.e. impaired strength) has been associated with decreased exercise capacity and increased severity of dyspnoea (Hamilton et al., 1995). Similarly, impaired respiratory muscle function has been implicated in difficulties weaning individuals following prolonged mechanical ventilation (Laghi et al., 2003) as well as in the development of alveolar hypoventilation and respiratory failure in individuals with spinal cord injury (Castriotta and Murthy, 2009), and conditions such as motor neuron disease, muscular dystrophy, Guillain–Barre syndrome and myasthenia gravis (Ambrosino et al., 2009). In the upper airway, dysfunction of the pharyngeal muscles is implicated in many conditions including snoring and obstructive sleep apnoea (OSA) (Horner, 2008), dysphagia (Miller, 2008), laryngeal aspiration (Miller, 2002), and speech disorders (Sonies, 1997).

Improved performance of the respiratory pump and upper airway muscles is the aim of specific muscle training programs, and is contingent on respiratory muscle loading having positive functional effects. The principle of eliciting a training-induced adaptation requires the muscles to be stressed (or loaded) to an extent that is greater than experienced during usual activities of daily living (American College of Sports Medicine, 2009). The nature of any adaptation is specific to the training load applied and the magnitude of change in muscle function is related to the training volume and frequency (American College of Sports Medicine, 2009). A characteristic of the adaptive response to increased loads is that any training-related improvements in muscle performance will decrease following cessation of training. The most commonly used loads for training the respiratory muscles are: (i) voluntarily ventilating at high levels for a prolonged periods (i.e. normocapnic hyperpnoea), (ii) resistive loading devices, and (iii) threshold loading devices (Hill et al., 2004).

The functional outcomes of respiratory muscle loading reflect changes, either positive or negative, at one or many points along the brain–muscle pathway, from the motor cortex to the muscle itself (see Fig. 1). A variety of sophisticated techniques have been used to provide insights regarding the response of these pathways to increased loads. This paper reviews our current knowledge of neurophysiological responses associated with acute and chronic loading of the respiratory pump and upper airway muscles.

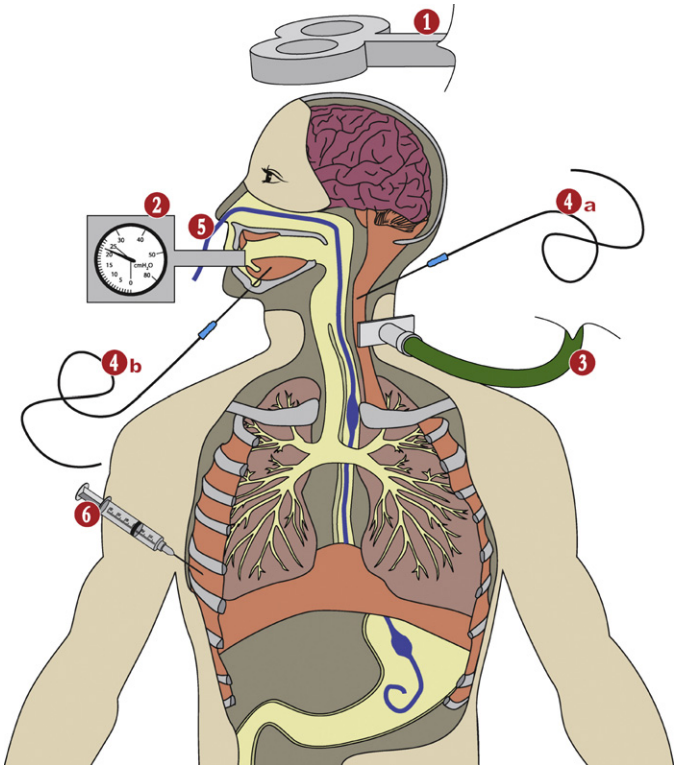

Fig. 1. Illustration of common techniques used to assess adaptations along the brain–muscle pathway in response to loading of the respiratory and upper airway muscles. 1: Transcranial magnetic stimulation. 2: Pressure manometer. 3: Magnetic phrenic nerve stimulation. 4a: Intramuscular EMG (sternocleidomastoid). 4b: Intramuscular EMG (genioglossus). 5: Gastric and oesophageal balloon catheters for the measurement of transdiaphragmatic pressure. 6: Muscle biopsy. Please note that structures in orange represent muscle, and not central nervous system tissue. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

2. Effects of acute loading

2.1. Reflexes

Reflex responses of the inspiratory muscles have been assessed using transient airway occlusion which effects a brief interruption to muscle shortening during contraction. Such occlusions produce an initial short-latency inhibitory response (35 ms) followed by long-latency excitation (105 ms), measured via electromyography (EMG) of muscles including the scalenes and parasternal intercostals (Butler et al., 1995). This differs from the load-compensating reflexes of limb muscles which are characterised only by excitatory responses (Marsden et al., 1976; Matthews, 1991). The initial inhibitory component of this inspiratory muscle reflex may serve as a protective mechanism during aspiration or inhalation of a foreign body to minimise the risk of further inhalation and airway collapse (Butler et al., 1995). While the precise function of the long-latency excitatory response is unclear, it may be analogous to the load-compensating reflexes in lower limb muscles which serve to maintain an upright posture against gravity (Zehr and Stein, 1999), and therefore in the setting of the respiratory muscles, this response may assist with maintaining ventilation following brief interruptions or airway occlusions. The response to occlusion of an intact upper airway is similar when the upper airway afferents are anaesthetised using topical lidocaine or bypassed via endotracheal intubation (Butler et al., 1995). It is also similar in patients with pulmonary denervation following heart–lung or bilateral lung transplantation (Butler et al., 1997), suggesting that motoneuron discharge in response to airway occlusion is mediated by receptors residing in the chest wall rather than the upper airways or intrathoracic structures. In contrast, the application of negative pressure to the airway has been shown to activate the pharyngeal dilator muscles (median latency ~34 ms), suggesting that upper airway and subglottal receptors may mediate genioglossus activity in some, but not all reflex responses (Horner et al., 1991).

2.2. Pre-activation

In healthy subjects, voluntary respiratory manoeuvers and the imposition of inspiratory resistive or threshold loads have been associated with electroencephalographic (EEG) activity prior to motor activation (Galgano and Froud, 2008; Macefield and Gandevia, 1991; Raux et al., 2007). The presence of pre-motor EEG activity, termed a Bereitschaftspotential (BP), often persists throughout periods of sustained inspiratory loading lasting for 60 min (Tremoureux et al., 2010). Such EEG activity suggests that inspiratory loading results in a state of expectancy or readiness