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Respiratory muscles during exercise: mechanics, energetics, and fatigue

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The respiratory muscles encompass a variety of functions and roles, their action during exercise facilitates arterial blood-gas and pH regulation. Exercise hyperpnea is the first line of defense to meet increased metabolic demand. In so doing, the muscles of respiration encounter several challenges, which may lead to respiratory muscle fatigue and impaired exercise tolerance. The focus of this brief review is to summarize recent developments in the study of respiratory muscle mechanics, energetics, and fatigue during exercise. Advances in the field are highlighted and directions of potential future research identified.

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Introduction

Air is pumped into and out of the lungs by rhythmic contraction of the respiratory muscles. Respiratory rhythm is tightly coupled with metabolic rate to ensure blood-gas and acid-base homeostasis. Several challenges to pulmonary ventilation exist during intense muscular exercise. First, alveolar ventilation ($\dot{V}_A$) must increase in proportion to muscular oxygen consumption ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$). Diffusion time for gaseous exchange at the alveolar-pulmonary capillary membrane is threatened by increased cardiac output. Second, exercise hyperpnea places substantial demands upon the respiratory muscles as breathing frequency (f_b), minute ventilation ($\dot{V}_E$) and the work of breathing (WOB) rise over time; breathing pattern and respiratory muscle recruitment strategies combine to reduce the metabolic cost of breathing. Third, contraction of the respiratory muscles increases the demand for blood flow and O_2 transport. As such, there is necessity for the gas transport needs of both respiratory and locomotor muscles to be considered. Failure to overcome these challenges may result in airflow limitation, dyspnea, hypoxemia, and respiratory muscle fatigue, ultimately leading to exercise intolerance. The central theme of the present review is to summarize the function of the respiratory muscles during exercise with respect to the challenges outlined above. We broadly focus our review on respiratory muscle: *i*) mechanics, *ii*) energetics, and *iii*) fatigue. The interested reader is directed elsewhere for a comprehensive review on the integrated neural control of exercise hyperpnea [1].

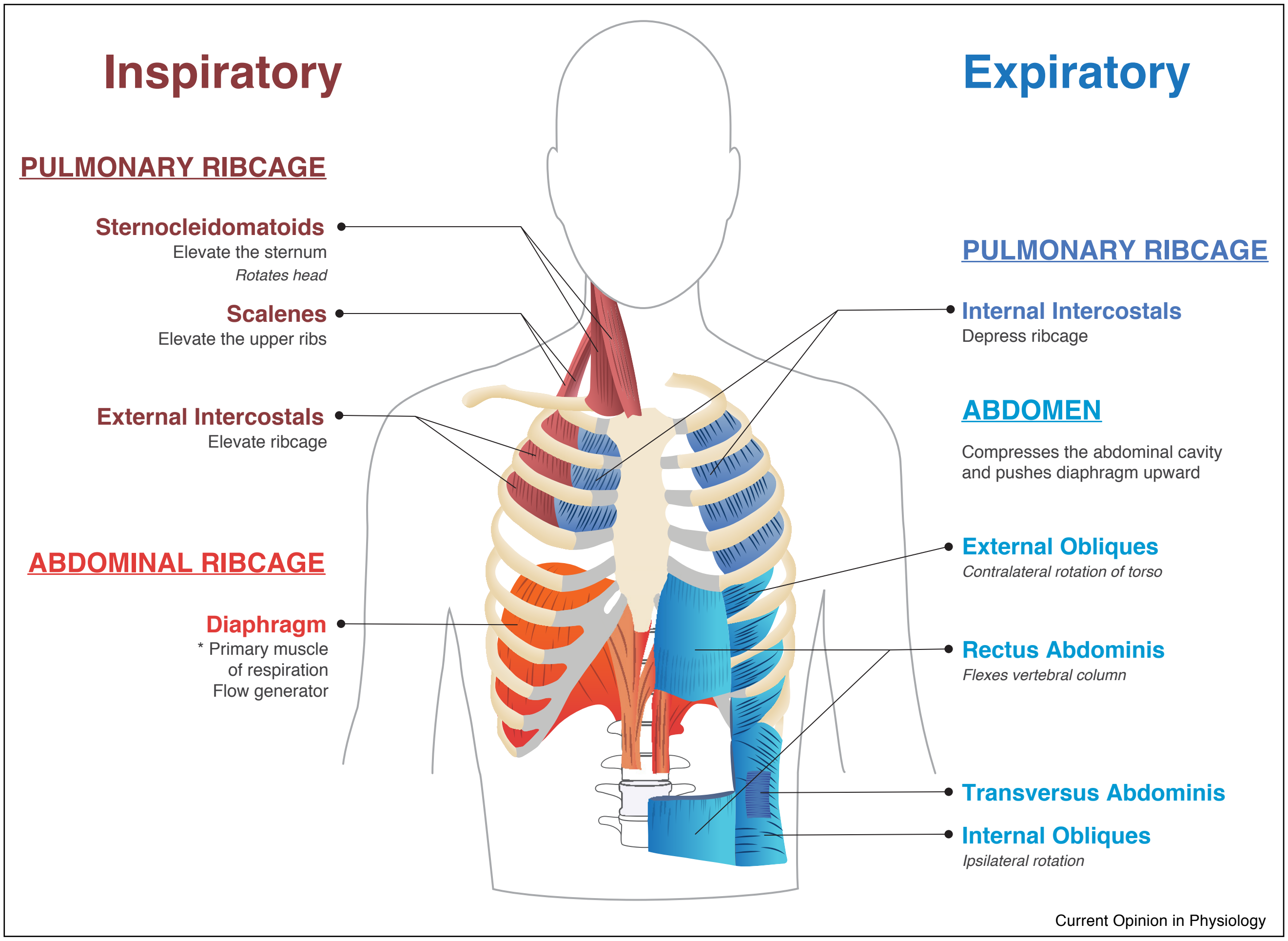
The respiratory muscles

The respiratory muscles can be functionally categorized into three groups: the diaphragm, the ribcage muscles and the abdominal muscles (for the purposes of this review, we shall not discuss laryngeal muscles, which are crucial in maintaining upper airway caliber and reducing resistance to airflow) (Figure 1). Pressure generated by the respiratory muscles during exercise has to overcome the flow-resistive, inertial, and viscoelastic properties of a dynamic respiratory system. The diaphragm contributes to roughly 70% of lung volume displacement during tidal breathing at rest. As exercise intensity increases, minute ventilation ($\dot{V}_E$) rises homologous to metabolic rate. A decrease in end-expiratory lung volume (EELV) and increase in end-inspiratory lung volume (EILV) accommodate changes in tidal volume (V_T) and $\dot{V}_E$. At peak exercise, V_T rarely exceeds 60% of vital capacity, leaving considerable ventilatory reserve. The transition from rest to peak exercise requires a pattern of respiratory muscle recruitment that optimizes lung and chest wall compliance in order to suppress dyspnea and minimize WOB in accordance with the principle of '*minimum effort*'. Furthermore, contractile properties, substrate utilization and muscle morphology of the respiratory muscles are well-suited for endurance-based tasks.

Mechanics

The mechanics of breathing is concerned with one basic question: how does air get into and out of the lungs? Contraction of the diaphragm generates tension within its fibers, displacing the central tendon caudally. Consequently: *a*) pleural pressure falls, allowing air to flow into the airways and alveoli, thereby increasing lung volume; *b*) abdominal pressure increases, pushing the abdominal cavity downward, allowing the thorax to expand; *c*) the ribcage is lifted upwards and outwards by action of the scalenes and sternocleidomastoid on the sternum, and

Figure 1



Major contributing respiratory muscles and their function.
Inspiratory (red) and Expiratory (blue) respiratory muscles, categorized by their respective compartments: pulmonary ribcage, abdominal ribcage, and abdomen. The primary respiratory action and non-respiratory action (italicized) are listed below each muscle or muscle group.

external intercostal muscles on the ribs. During incremental exercise, there is a progressive increase in V_T, which can be achieved by different configurations of the ribcage and abdomen. Between the transition from rest to moderate-intensity exercise, the ribcage contributes little to volume displacement, whereas during moderate-intensity to high-intensity exercise, the ribcage contributes significantly. It was originally believed that the recruitment of accessory and obligatory inspiratory muscles assisted the diaphragm in order to elevate lung volume. This premise however, is limited by the assumption of a rigid ribcage, moving with only two degrees of freedom.

Alternative models [2] separate ribcage involvement to volume displacement into its constituent compartments — the pulmonary/upper ribcage (apposed to the lung) and the abdominal/lower ribcage (apposed to the diaphragm), thus creating a three-compartmental model of chest wall kinematics. The mechanical arrangement of the diaphragm and ribcage muscles are presented in parallel. Therefore, V_T can be partitioned into a component due to contraction of the ribcage muscles and a second component due to diaphragmatic contraction. The diaphragm acts upon the abdominal ribcage [3], whereas, inspiratory and expiratory ribcage muscles act upon the pulmonary ribcage [4].

Modern investigations of respiratory mechanics have employed optoelectronic plethysmography (OEP) to provide information on breath-by-breath adjustments of the entire chest wall (including its ribcage and abdominal compartments) during exercise [5]. In short, reflective markers are positioned on anatomical reference sites of the ribcage and abdomen. Infrared cameras locate the markers and relay three-dimensional co-ordinates to a computer for motion analysis [6]. Using this method, coalesced with ancillary measures of respiratory breathing pressures (esophageal/pleural and gastric/abdominal pressure), Aliverti *et al.* [7] were able to distinguish the pressures generated by each respiratory muscle group. Where the ribcage muscles aim to displace the pulmonary ribcage to increase EILV, the abdominal muscles decrease EELV by displacing the abdomen, situating the diaphragm on a more advantageous portion of its length-tension curve [8•] (Figure 2). Should changes in respiratory muscle length and/or tension be insufficient for the outgoing motor command, dyspnea ensues. Notwithstanding the salient, yet underappreciated postural role of the abdominal muscles (among others), loss of abdominal tone has significant effects on operating lung volumes and diaphragm pressure production in spinal cord injury [9].

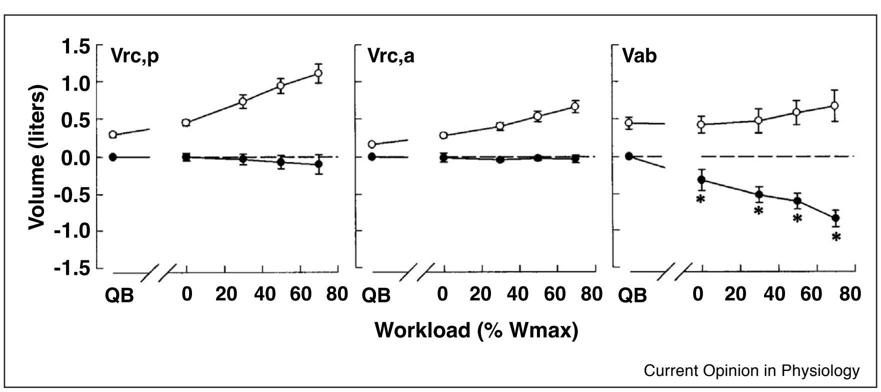
In combination with computed tomography denoting clear sex differences in lung size, shape and kinematics [10•], measurements of respiratory muscle electrical activity suggests that women rely more upon inspiratory neck and ribcage muscles during submaximal exercise compared to men [11]. It is posited that greater ribcage inclination accommodates a larger abdominal volume to assist parturiency [12], while sparing diaphragmatic work. Three-dimensional measurements (i.e. OEP) of the chest wall during exercise may confirm the notion of sex differences in respiratory mechanics, but are currently inconclusive [13]. With aging, progressive loss of elastic recoil pressure leads to reduced ventilatory capacity such that during incremental exercise, operating lung volumes are elevated, dyspnea heightened and flow limitation more frequent [14], which corresponds to increased WOB [15]. Of note, a recent study found mechanical ventilatory constraints do not influence the perception of dyspnea in healthy older individuals during cycle exercise at ventilatory threshold, implying a non-physiological genesis [16••]. The contribution of the different respiratory muscle groups to pressure–volume relationships of the lung and chest wall directly influence mechanical efficiency and enthalpy.

Energetics

Energetics refers to the supply of chemical energy to the respiratory muscles from sources available within the muscles or blood. The respiratory muscles, akin to those of locomotion, require substantial increases in O_2 transport and blood flow to sustain contraction during exercise. Experiments of respiratory muscle energetics require careful attention to pressures, volumes and flows due to neurohumoral differences between reflexively driven and voluntarily driven hyperpnea, where small errors can inflate the O_2 cost [17]. Subjects are instrumented with a gastro-esophageal balloon catheter during a bout of exercise. On subsequent experimental days, subjects sit quietly and replicate the breathing pattern (V_T, f_b, $\dot{V}_E$, duty cycle) and respiratory pressures associated with their exercise hyperpnea. Respiratory muscle $\dot{V}O_2$ ($\dot{V}O_{2RM}$) is calculated as the difference between the $\dot{V}O_2$ elicited by exercise and voluntary hyperpnea. There is now general consensus that during maximal exercise, $\dot{V}O_{2RM}$ comprises approximately 10% of total $\dot{V}O_2$ ($\dot{V}O_{2max}$) in the untrained healthy subject and 15–16% in the highly trained ($\sim$300–500 ml min^{-1}) [18], with values as high as 35–40% in those with chronic obstructive pulmonary disease [19]. What is more, the O_2 cost [20•] and mechanical WOB [21,22] is higher in women than men, assumed to be related to dysanapsis of the airways and lungs [23]. Lastly, $\dot{V}O_{2RM}$ constitutes a larger fraction of the slow-component of $\dot{V}O_2$ during severe exercise intensities relative to heavy exercise, owing to exponential increases in WOB [24].

An increase in $\dot{V}O_{2RM}$ must be accompanied by an increase in respiratory muscle perfusion. There are inherent limitations to measuring human respiratory muscle blood flow due to the complex vascular network and anatomical arrangement of the respiratory musculature.

Figure 2



Nonetheless, collective data from different experimental approaches and species, indicate that diaphragmatic blood flow commands ~14–20% of maximal or near-maximal cardiac output ($\dot{Q}$, ~250–350 ml min^{-1} 100 g^{-1}, or 120 cal min^{-1} at a $\dot{V}_E$ of 120 l min^{-1}) [25,26••], significantly greater than any other respiratory muscle and most other skeletal muscles. Extensive blood supply networks (tributaries from phrenic, internal thoracic and intercostal arteries) to the diaphragm supports its high blood flow capacity, with the majority of muscle fibers being oxidative (to our knowledge sex differences in respiratory muscle histochemistry have not been studied). In heart failure, diaphragm blood flow is nearly double that of control values, even during submaximal exercise [27], possibly due to the effects of pulmonary congestion on dynamic lung compliance. Limitations to respiratory muscle blood flow do exist once a critical tension-time index of 0.20 is reached, culminating in contractile failure (i.e. fatigue).

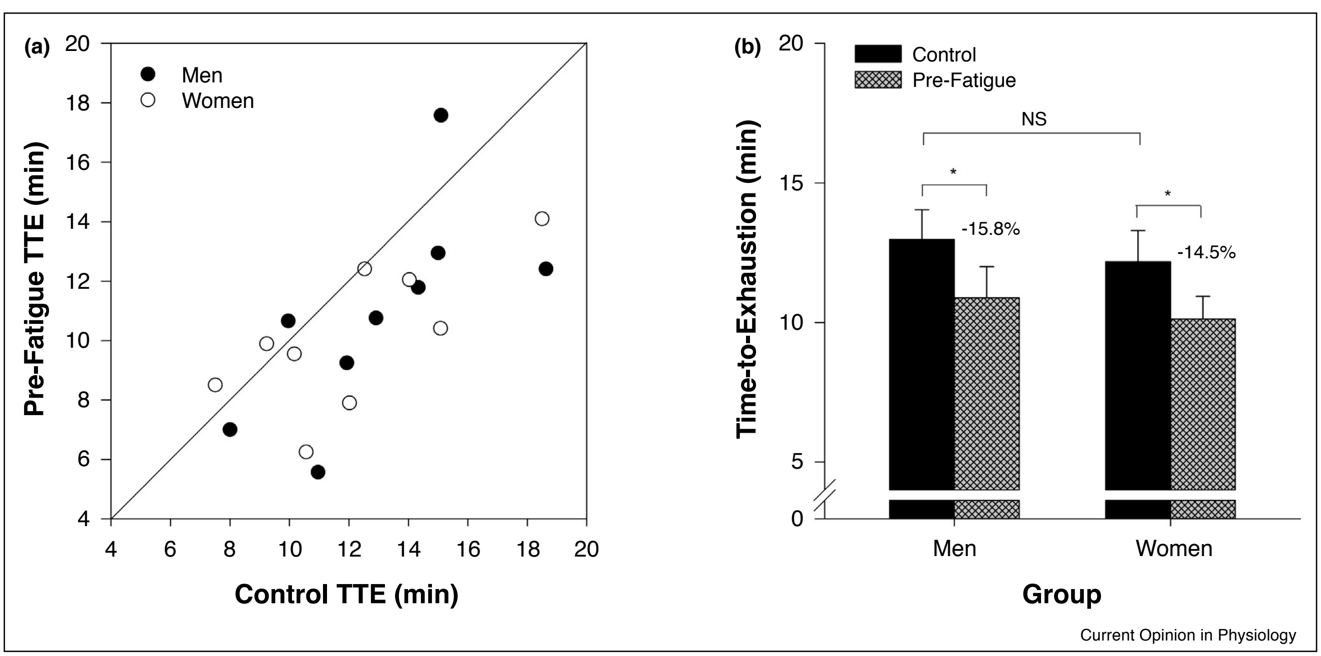
Fatigue

Muscular fatigue is defined as a temporary condition, in which there is a decrease in the capacity of muscle force generation that is reversible by rest. Despite possessing excellent endurance characteristics, the muscles of respiration are prone to fatigue should energy demand exceed supply. Sources that determine energy demands include: *a*) WOB, *b*) respiratory muscle strength, and *c*) efficiency. Sources of energy supply include: *a*) arterial O_2 content, *b*) respiratory muscle blood flow, *c*) blood substrate concentration, *d*) energy stores, and *e*) ability to extract energy sources. The balance between these factors determine the presence of respiratory muscle fatigue.

During intense physical activity ≥85% $\dot{V}O_{2max}$, the respiratory muscles fatigue [28–31]. Recent evidence has shown that the development of fatigue is progressive and linked with the cumulative WOB [32•]. In line with this conjecture, manipulating WOB using resistors or proportional assist ventilation, alters the severity of exercise-induced diaphragmatic fatigue in proportion to the change in WOB — with increased work leading to augmented fatigue [33]. Fatigue of the respiratory muscles does not occur during voluntary hyperpnea mimicking exercise ventilation [34], suggesting that blood flow competition/limitation contributes to fatigue development. Interestingly, high-intensity whole-body exercise at sea-level does not induce significant diaphragmatic fatigue in most healthy young women [35].

Inspiratory [36] and expiratory [37] muscle fatigue elicits a sympathetically mediated metaboreflex, resulting in locomotor and respiratory muscle hemodynamic alterations. A detailed review of this complex phenomenon can be found elsewhere [25]. Activation of metabolically

Figure 3



Effect of diaphragm fatigue on subsequent exercise tolerance.
Adapted from Welch *et al.* [48••]. **(a)** Change in exercise tolerance with prior-induced diaphragmatic fatigue compared to a control trial in men (filled circles) and women (open circles). **(b)** Control (filled bars) and pre-fatigue (hatched bars) time-to-exhaustion exercise times in men and women.

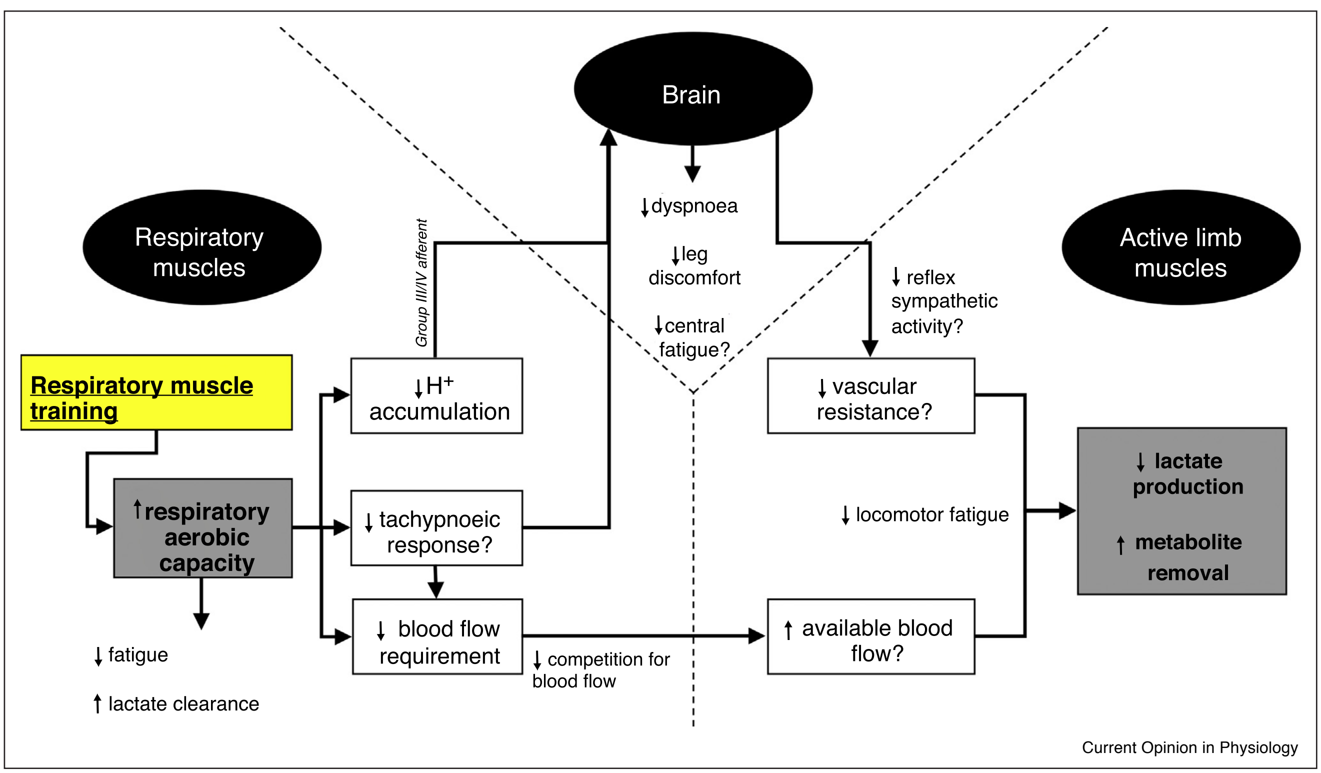
and mechanically sensitive group III/IV afferents produces widespread time-dependent sympathetic vasoconstriction. Increasing or decreasing respiratory muscle work above or below the normally occurring WOB during dynamic exercise (between 40–80% of peak workload) causes a commensurate change in median nerve muscle sympathetic activity (MSNA) [38,39••,40•] and blood flow to the active and inactive limb (during submaximal and maximal exercise) [41,42••], where $\dot{Q}$ is believed to be preferentially redistributed to the respiratory muscles [43]. It stands to reason that the reciprocal also be true — that fatiguing locomotor work reflexively educes vasoconstriction of the respiratory muscle vasculature, though this postulate has yet to be demonstrated. The reduced sensitivity of adrenergic receptors to noradrenaline in diaphragm arterioles relative to the gastrocnemius muscle may indicate that the respiratory muscles 'steal' blood away from locomotor muscles [44]. During low-moderate intensity cycling exercise with inspiratory resistance, it has recently been found that the increase in MSNA is blunted in women compared to men [40•], likely further evidence of an attenuated inspiratory muscle metaboreflex observed in young women during isolated flow-resistive or pressure-threshold loading tasks [45••,46]. Whether such sex differences remain during tasks of equal absolute diaphragmatic work is not known (i.e. sex versus size).

Both inspiratory [47,48••] and expiratory [49] muscle fatigue impairs exercise capacity through the aforementioned cardiovascular consequences and heightened perceptions of breathlessness. As a result of reduced O_2 delivery to the active limb locomotor muscles, quadriceps fatigue is hastened and exercise prematurely terminated [50]. Group III/IV muscle afferent feedback modulates central motor drive (i.e. central fatigue) via $GABA_B$ neuron-mediated inhibition [51]. Inducing fatigue of the inspiratory muscles before whole-body exercise yields a ~15% reduction in exercise tolerance, independent of sex, as shown in Figure 3.

Exercise performance

To address the question of whether or not the effects of respiratory muscle work influence exercise performance, a number of studies have artificially altered the work of the inspiratory muscles during exercise. By unloading the respiratory muscles up to 50% below the normally occurring WOB: *i*) diaphragm fatigue is prevented, *ii*) locomotor muscle fatigue at end-exercise is reduced by 25–30% of control values, and *iii*) exercise duration to exhaustion

Figure 4



is prolonged 10–20% in healthy subjects in normoxia or acute hypoxia, and in patients with congestive heart failure [52]. The performance related improvements associated with unloading can be attributed to changes in leg blood flow. We emphasize that the above-mentioned effects of respiratory muscle unloading occur only during high-intensity exercise.

Respiratory muscle training (RMT) is a means to specifically target the respiratory musculature and possibly improve exercise tolerance/performance. A host of functional outcomes have been linked with RMT, including reduced sensation of dyspnea [53], mitigation of respiratory [54] and locomotor [55] muscle fatigue, and improved exercise capacity [56•]. The mechanisms by which specific RMT programs may facilitate improvements in exercise tolerance and/or performance are speculated upon in Figure 4. Despite a strong theoretical rationale and an abundance of research supporting its use, mechanistic studies investigating the physiological adaptations that occur with training are sparse.

Conclusion

Vital to the regulation of blood-gas homeostasis during exercise, the ventilatory pump muscles work in unison to co-ordinate changes in pleural pressure, inspiratory and expiratory flow, lung volume, and aeration. The mechanics of breathing are well understood, but newer techniques and revelations regarding differences between the sexes and changes that occur with healthy aging continue to advance our understanding of respiratory muscle function during exercise. Exercise hyperpnea precipitates a high demand for respiratory muscle blood flow and O_2 delivery, which may lead to fatigue. Inspiratory and expiratory muscle fatigue contributes to exercise impairment — RMT strategies may allay this effect.

Conflicts of interest statement

Nothing declared.

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Author contributions

J.F.W., S.K., and A.W.S. contributed to drafting and critically revising the manuscript. All authors approved the final version of the manuscript.

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