PERSPECTIVES

Cardiorespiratory responses to exercise in CHF: a conspiracy of maladaptation

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Chronic heart failure (CHF) patients have markedly impaired exercise performance in the face of reduced cardiac output, augmented sympathetically mediated systemic vasoconstriction and an excessive hyperventilation secondary to inefficient pulmonary gas exchange and excessive drive to breathe. Olson *et al.* in a recent article in *The Journal of Physiology* (Olson *et al.* 2010) have now shed light on this complex, maladaptive response in CHF by demonstrating that these patients experienced marked increases in stroke volume and cardiac output, and in limb vascular conductance and blood flow, during submaximal exercise when their work of breathing (WOB) was reduced via a mechanical ventilator (MV). There is much to be admired in their experimental design, including use of thermal dilution measures of limb blood flow and oesophageal pressures to quantify WOB. Furthermore, the use of MV to unload the respiratory muscles served to unmask the cardiovascular effects of the normally occurring excessive WOB in these difficult-to-study patients.

The increased limb vascular conductance with respiratory muscle unloading is similar in direction (but smaller in magnitude) to that reported in healthy athletes; however, in the CHF patients this effect occurred at only 60% maximum exercise, whereas in health, near-maximum exercise was required to produce sufficient WOB to elicit any cardiovascular effects of respiratory muscle unloading (Dempsey *et al.* 2006). The augmented stroke volume (SV) and cardiac output observed with reduced inspiratory negative pleural pressure in CHF is opposite in direction to that reported in healthy humans and animals, apparently reflecting a critical dependency of SV on ventricular preload in health and on after-load in CHF. If the observed increase in limb blood flow with unloading does indeed imply a 'steal' of flow from the limbs by the diaphragm (which to date has been reported only in a rodent model of CHF), then this shift would probably require (a) activation of respiratory muscle metaboreflexes acting via type III–IV phrenic afferents (Dempsey *et al.* 2006) for feedback regulation of sympathetic vasoconstrictor outflow, plus (b) a marked difference in vasoconstrictor sensitivity of phrenic arterioles *vs.* those in limb musculature in response to noradrenaline (norepinephrine) (Aaker & Laughlin, 2002). However, we should not presume that the diaphragm is receiving all of the blood flow it requires during whole body exercise; to the contrary, the diaphragm fatigues during high intensity endurance exercise, but does not fatigue when the same high WOB is sustained voluntarily in a resting subject (Dempsey *et al.* 2006). These data imply that a strong competition for blood flow between respiratory and limb skeletal muscles does indeed prevail during exercise of heavy intensity. Studies are now required to provide more direct evidence of how alterations in the work of breathing alter this flow distribution between locomotor muscles and those of the chest and abdominal wall during exercise. We also need to determine the mechanisms responsible for activation of respiratory muscle metaboreflexes and, in turn, selective sympathetically mediated vasoconstriction.

There are several potential sources of the augmented drive to breathe in CHF. Recent findings in animal models of CHF report upregulation at the level of the carotid chemoreceptor as a key source of both augmented ventilatory and sympathetic drives both at rest (Ding *et al.* 2008) and especially during exercise (Stickland *et al.* 2007). One of the links of WOB to limb blood flow and in turn, to exercise performance may be found in the reduced exercise-induced quadriceps fatigue obtained when WOB was reduced via MV during near-maximum exercise in health and during sub-maximum exercise in hypoxia or in patients with chronic obstructive pulmonary disease (COPD) (Amann *et al.* 2010). In turn, a clinical implication of Olson *et al.*'s findings would be the use of respiratory muscle unloading together with supplemental O_2 in rehabilitation of exercising CHF patients, in order to reduce sympathetic vasoconstriction and effort perception, thereby promoting increased work rates and allowing a greater locomotor muscle training effect to be achieved. Finally it is common clinical practice to contrast an exercising patient's specific perceptions of dyspnoea *vs.* those of limb muscle discomfort to identify the source of exercise performance limitation (i.e. respiratory *vs.* limb muscle). However, given the dependence of limb blood flow and O_2 transport, fatigue and effort perception on the work of breathing as shown by Olson *et al.* and in related studies (Dempsey *et al.* 2006; Amann *et al.* 2010), this practice is likely to be highly misleading.

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DOI: 10.1113/jphysiol.2010.193805