

PERSPECTIVES

Insights into the role of the respiratory muscle metaboreflex

Craig A. Harms

Department of Kinesiology, Kansas State University, Manhattan, KS 66506, USA

Email: caharms@ksu.edu

Factors affecting exercise tolerance have been of interest to respiratory physiologists for several decades. Among these limiting factors is diaphragmatic fatigue, which occurs during sustained exercise of high intensities ($> 80\%$ maximal oxygen consumption ($\dot{V}_{O_{2,max}}$)) (Babcock *et al.* 1995). Exercise-induced diaphragmatic fatigue is, in part, due to the high levels of respiratory muscle work that must be sustained throughout high intensity exercise. The consequences of a fatiguing diaphragm and other respiratory muscles have been addressed in a recent review by Dempsey *et al.* (2006). Briefly, recent reports have suggested that accumulation of metabolites in the inspiratory and expiratory muscles when respiratory muscles are fatigued activates unmyelinated type IV phrenic afferents (Hill, 2000), which in turn increases sympathetic vasoconstrictor activity via a supra-spinal reflex. Why is this reflex effect important during exercise? During strenuous exercise, when the work of breathing is reduced by $\sim 50\%$ via proportional assist ventilation in healthy subjects, cardiac output is reduced and vascular conductance and blood flow to the exercising legs are increased and whole body exercise performance increases (Harms *et al.* 1997, 2000). Presently, it is not known what specific mechanisms activate the respiratory muscle metaboreflex sufficiently to increase sympathetic vasoconstrictor activity and affect cardiovascular indices.

In the current issue of *The Journal of Physiology*, Witt *et al.* (2007) provide significant insight into the role of the respiratory muscle metaboreflex on cardiovascular consequences during heavy exercise. These researchers utilized five weeks of inspiratory muscle training (IMT) in an attempt to

increase respiratory muscle strength and presumably reduce or delay respiratory muscle fatigue. In this study, IMT reduced the increase in heart rate and mean arterial pressure that typically occurs with the increased work of breathing during heavy exercise in healthy subjects. What was the mechanism for this reduced cardiovascular responsiveness to high levels of inspiratory work? The authors speculated that the decreased cardiovascular response was due to: (a) reduced activity of chemically sensitive afferent fibres innervating the inspiratory muscles or to a desensitization, or (b) a decline in responsiveness of the type III and IV afferents to chemical stimulants resulting from a conditioned response to repeated exposure to the accumulated metabolites associated with IMT, although either mechanism has yet to be established.

The significance of these findings by Witt *et al.* (2007) addresses broader questions of the importance of respiratory muscle work to exercise performance. Recent studies have demonstrated that the respiratory muscle metaboreflex is a key player in increased sympathetic tone and blood flow redistribution during heavy exercise (Sheel *et al.* 2001; Rodman *et al.* 2003). Importantly, there appears to be a threshold for activation of this reflex that does not occur during exercise of low to moderate intensities or non-fatiguing inspiratory efforts. The authors suggest that IMT may have raised the threshold required to elicit significant increases in mean arterial pressure. Future work is necessary to determine specifically how increases in inspiratory muscle strength led to these improvements.

Additionally, inspiratory muscle training has received considerable interest and enthusiasm in recent years as a method to improve whole body exercise performance in healthy subjects. However, to date, the literature appears inconclusive. This may be due in part to differences in training strategies, subject populations or inappropriate control groups. In those studies that have shown significant gains in performance, mechanisms responsible are still unresolved. Results from the present study of Witt *et al.* (2007)

provide novel insights into a potential role of the metaboreflex for the possible benefit of IMT. Reduced cardiovascular responsiveness to high levels of inspiratory muscle work with IMT in this study points to a plausible explanation for the improvements in exercise performance with IMT. Alternatively, IMT has often been shown to be an effective tool for patients with chronic obstructive pulmonary disease (COPD) and congestive heart failure (CHF). Based on Witt *et al.* (2007), future studies investigating the role of IMT on the inspiratory muscle metaboreflex could help determine the mechanistic basis for the improvements in this population.

In summary, Witt *et al.* (2007) have provided a significant step forward in our understanding of the inspiratory muscle metaboreflex by their careful, quantitative approach in determining the mechanisms responsible for the cardiovascular responses that occur with respiratory muscle work during strenuous exercise. The results from this study substantiate the importance of this reflex to competing vascular beds in healthy subjects during high intensity exercise. Hopefully, these findings will provide an impetus for further, insightful investigations into the cardiopulmonary consequences of respiratory muscle work during exercise.

References

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