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CROSSTALK

## CrossTalk opposing view: Respiratory muscle training does improve exercise tolerance

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In the vast majority of healthy human beings exercising at sea level, there is no respiratory limitation to oxygen uptake. This fact leads inevitably to the question, how can respiratory muscle training (RMT) possibly improve exercise tolerance? Resolution of this conundrum lies in thinking beyond the obvious, and in an appreciation of the role of respiratory muscle work in perfusion and neural fatigue mechanisms.

In a recent systematic review and meta-analysis of RMT, Illi and colleagues (Illi *et al.* 2012) undertook a detailed analysis of some 46 original studies of RMT. The analysis included both strength and endurance RMT, and sought to (1) identify factors that influence changes in exercise tolerance after RMT and (2) undertake a meta-analysis of a sample of placebo and controlled trials ($n = 8$). The meta-analysis revealed 'significant improvement in performance after RMT, which was detected by constant load tests, time trials and intermittent incremental tests, but not by [continuous] incremental tests'; standardised mean differences were 0.66, 1.85, 2.96 and 0.3, respectively (Illi *et al.* 2012).

Of course, one can contend the validity of the conclusions of any meta-analysis on the basis of the rigour applied to inclusion criteria, and the relevance/validity of the key outcome variables (Polkey *et al.* 2011). The argument that RMT simply makes people better at doing volitional tests of respiratory muscle function has been invoked previously (Polkey *et al.* 2011); indeed, my adversary has argued strongly that the inability to measure significant increases in diaphragm twitch pressures (Tw Pdi) following RMT divests the intervention of all credibility, stating that, '234 subjects would need to be randomized to definitively refute the hypothesis that [RMT] improves Tw Pdi and we argue that such a study is required' (Hart *et al.* 2001). In addition to the obvious limitation of Tw Pdi for assessing the outcome of RMT (i.e. poor between-day reliability), recent advances in the understanding of exercise limiting factors (see below) also highlight the inadequacy of reductionist approaches to evaluating complex, integrative physiological phenomena.

Thus, if one accepts the robustness of Illi and colleagues' methods (Illi *et al.* 2012), their recent meta-analysis provides strong, objective support for the contention that RMT improves exercise tolerance. Notwithstanding this, the credibility of RMT resides ultimately in the provision of convincing underlying mechanisms for resulting changes in exercise tolerance. In this regard, I contend that RMT has also achieved a critical threshold of credibility (McConnell, 2007). As mentioned previously, the key to understanding how RMT influences exercise tolerance is an appreciation of the role of respiratory muscle work in perfusion, and in central and spinal mechanisms of fatigue.

The role of respiratory muscle work in exercise limitation has been studied extensively by Dempsey and colleagues who have made an outstanding contribution to our understanding of interactions between muscle afferents (respiratory and locomotor), and a range of factors that limit exercise tolerance. Specifically, Dempsey's group has elucidated the respiratory muscle metaboreflex, which elicits sympathetically mediated vasoconstriction (Harms *et al.* 1997; Dempsey *et al.* 2006). Above a critical threshold of inspiratory muscle work, the accumulation of metabolites within exercising respiratory muscles stimulates group III and IV afferents, inducing sympathoexcitation (Sheel *et al.* 2002). Functional repercussions include accelerated time to fatigue during exercise (Harms *et al.* 2000; McConnell & Lomax, 2006), and exacerbation of exercise-induced locomotor muscle fatigue (Romer *et al.* 2006). Subsequently, we, and others, have shown that specific inspiratory muscle training increases the intensity of inspiratory muscle work required to activate this reflex (McConnell & Lomax, 2006; Witt *et al.* 2007; Chiappa *et al.* 2008). Whilst remaining circumstantial, these findings point to RMT exerting an influence upon exercise tolerance by increasing the intensity of inspiratory muscle work required to stimulate group III and IV afferents. This effect may be mediated in part by an increase in the efficiency of the respiratory pump (Turner *et al.* 2012), but also by a phenomenon demonstrated recently in limb muscles, whereby limb training attenuates the decline in muscle blood flow during exhaustive exercise (Rud *et al.* 2012). Since respiratory muscle blood flow also declines above 80% of peak work rate (Vogiatzis *et al.* 2009), it is reasonable to suggest that RMT may attenuate this response, preserving respiratory muscle blood flow. Thus, RMT creates a 'virtuous circle' in which preservation of respiratory muscle blood flow reduces metabolite accumulation, delays stimulation of group III and IV afferents, and reduces sympathoexcitation.

Group III and IV fibres project to a number of sites within the central nervous system. Most recently, Amann and colleagues employed a selective $\mu$-opioid receptor agonist to demonstrate, for the first time, that afferent feedback from locomotor group III and IV fibres makes an 'essential contribution' to both cardiorespiratory control and perceptual responses in the exercising human being (Amann *et al.* 2010). The latter finding is consistent with the observation that RMT attenuates both respiratory and peripheral effort perception (Romer *et al.* 2002), which may arise because of reduced feedback from group III and IV afferents in both respiratory and locomotor muscles.

**Alison McConnell** graduated from the University of Birmingham with a BSc in Biological Sciences (Physiology). Her transition into exercise physiology came after completing an MSc in Human and Applied Physiology, and a PhD at King's College London. Alison joined Brunel University in 2000 where she has pursued her interest in respiratory limitations to exercise. In particular, she has pioneered research on the ergogenic influence of inspiratory muscle training. Her guide to breathing training for sport, 'Breathe Strong, Perform Better', was published by Human Kinetics Inc. in 2011, and a guide for clinicians will be published by Reed Elsevier in Spring 2013.


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Furthermore, feedback from group III and IV afferents is also implicated in central fatigue mechanisms, via inhibition of central motor output (Gandevia, 2001). It has been suggested that afferent feedback from exercising muscles protects locomotor and respiratory muscles from catastrophic fatigue (Gandevia, 2001). Indeed, Gandevia suggested, 'An extreme example [of central fatigue] occurs with exercise of the inspiratory muscles in which task failure can occur with minimal peripheral fatigue' (Gandevia, 2001). This underscores the folly of reductionist models to infer the contribution, or otherwise, of a specific system component in exercise limitation. The importance of group III and IV afferent feedback in regulating integrated exercise responses was illustrated recently by a study in which a cycle time trial was undertaken with and without the selective $\mu$-opioid receptor agonist fentanyl (Amann *et al.* 2009). During a self-paced 5 k time trial, intrathecal fentanyl was associated with greater quadriceps fatigue, a higher central motor output, and greater perceived exertion, compared with placebo. A higher power output in the first half of the fentanyl time trial was offset by a lower power output in the second, resulting in no change in performance time. However, compared with placebo, the decline in quadriceps twitch force was greater with fentanyl (45.6% *vs.* 33.1%) and was associated with ambulatory problems post-exercise. The authors suggest their data, 'emphasize the critical role of locomotor muscle afferents in determining the subject's choice of the "optimal" exercise intensity that will allow for maximal performance while preserving a certain level of locomotor muscle "functional reserve" at end-exercise' (Amann *et al.* 2009). The specific contribution of respiratory muscle group III and IV afferents to central fatigue during whole body exercise awaits investigation. Given the importance of protecting diaphragm function, it is reasonable to speculate that the inhibitory feedback from diaphragm afferents during exercise influences both respiratory and locomotor central motor output.

Thus, training-induced alterations in group III and IV afferent feedback from respiratory muscles most likely enhance exercise tolerance at multiple loci, and exploration of this possibility creates new and exciting avenues for future research. Accordingly, rather than pondering *if* RMT improves exercise tolerance, the focus should fall upon *how* RMT improves exercise tolerance, for this will provide the key to unlocking its full potential.

## Call for comments

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Questions about this call should be directed to Jerry Dempsey at jdempsey@wisc.edu.

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### Conflict of interest

The author is an inventor of two inspiratory muscle training products and acknowledges a beneficial interest in the form of a share of licence income to the University of Birmingham and Brunel University. She also acts as a consultant to POWERbreathe International Ltd.