1	The misuse of respiratory resistive loading during aerobic exercises: revisiting
2	mechanisms of "standalone" inspiratory muscle training
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#### 35 Introduction

36 The application of "standalone" respiratory muscle training (RMT) to clinical 37 and athletic populations is now supported by a plethora of systematic reviews and meta-38 analyses supporting its benefits (1). The most commonly applied method of RMT adopts the principles of strength training, whereby brief bouts of moderate intensity 39 40 respiratory loading (40 to 60% of maximal strength) are applied, resulting variously in improvements in respiratory muscle strength, power, shortening velocity and endurance 41 42 (2). Among RMT modalities, inspiratory muscle training (IMT) is the most commonly 43 employed method for healthy (1,3) and clinical (4,5) populations. A typical IMT 44 intervention consists in breathing against an inspiratory load (IRL), twice daily, for five to seven days per week, for four to twelve weeks (3,4,5). Recently, a high-intensity 45 inspiratory muscle strength training (IMST) protocol that required 30 breaths (~5 46 47 minutes) per session, for 5 to 7 days (25–35 total minutes) per week for 6 weeks, reduced resting blood pressure in young healthy adults (6), in midlife/older adults (7), 48 49 and older adults with obstructive sleep apnoea (OSA) (8). Behind its mechanisms, 50 IMST improved endothelial function, NO bioavailability, and oxidative stress (7), and 51 reduced muscle sympathetic nerve activity (8).

IMT has been included as a component of exercise-based cardiopulmonary rehabilitation programmes. Indeed, randomized controlled trials (RCTs) suggested an additive effect of inspiratory muscle training (IMT) and aerobic exercise (AE) training in chronic heart failure (CHF) and chronic obstructive pulmonary diseases (COPD) if conducted in independent sessions (9,10). IMT plus AE training improved cardiorespiratory responses to exercise in CHF (9) while providing additional gains in endurance time and reduced dyspnoea in COPD (10).

However, no study supports the inspiratory loading use during AE in either sporting or clinical populations. In this research letter, we revisit putative mechanisms underlying the established benefits of "standalone" IMT in order to support our contention that IMT need not and should not be used during AE sessions.

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# 64 Mechanism 1: The respiratory muscle metaboreflex

During heavy-intensity exercise, respiratory muscle work requires an average of https://www.exercise.com/competing/for/blood flow (e.g., oxygen and nutrients) with locomotor muscles. The mechanism by which blood flow competition arises is suggested to occur via the so-called "respiratory muscle metaboreflex" (11), 69 whereby fatiguing activity of the inspiratory muscles leads to accumulation of 70 metabolites, which stimulate unmyelinated afferents. This stimulation induces a 71 sympathetically-mediated vasoconstriction within limb locomotor muscles (12), which 72 hastens locomotor muscle fatigue and exercise limitation (12) and intensifying effort 73 perceptions. IMT has been shown to increases the threshold for respiratory 74 metaboreflex activation in healthy (13) and patients with heart failure (5), thereby 75 improving exercise tolerance.

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### 77 Mechanism 2: Reduced respiratory and locomotor effort perceptions

78 The hypothesis that IMT improves exercise performance may be explained, in 79 part, by the reduced respiratory and whole body effort perceptions in athletes (14) and clinical populations (4) after IMT. The reduced dyspnoea seems to be associated with 80 81 improvements in the force-generating capacity of inspiratory muscles after IMT, which 82 decreases the relative tension for a given level of ventilation (4). During conditions 83 where elevated ventilation is needed, such as exercise, this adaptation from inspiratory 84 muscles most likely underpins the diminished respiratory effort (4). IMT also reduces 85 peripheral effort sensations (14) probably via a reduction in respiratory muscle blood 86 flow needs and a boosting of oxygen delivery and metabolite removal from to the limbs.

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### 88 Mechanism 3: Reduced oxygen cost of breathing

The oxygen cost of breathing is related directly to the energy requirement of the respiratory muscles. IMT reduces the oxygen cost of breathing for a given ventilatory requirement during voluntary hyperphoea post-IMT (15). Specifically, in highly trained cyclists, IMT reduced the oxygen cost of breathing at ventilations above 50% of the maximal oxygen uptake (15). It suggests that IMT, at least in this population, reduces the energy demand from respiratory muscles during hyperphoea.

Thus, in trained individuals, a reduced oxygen cost of breathing most likely contributes to exercise performance improvements following IMT by reducing their demand for oxygen, thereby liberating oxygen for use by locomotor muscles. To our knowledge, this mechanism has yet to be evaluated in clinical populations.

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#### 100 Mechanism 4: Attenuation of central fatigue

Lastly, we proffer an as yet untested mechanism underpinning the ergogeniceffect of IMT. Exercise intolerance is elicited by a number of interrelated peripheral

103 factors, but is also affected by so-called "central fatigue", which is driven by feedback 104 from muscle afferents (16). To date, the focus of attention has been upon feedback 105 originating from locomotor muscles; however, feedback from the respiratory muscles 106 almost certainly contributes to the ensemble of inputs influencing central motor drive. 107 Accordingly, we suggest that attenuation of respiratory muscle afferent feedback 108 following IMT might delay, or attenuate, central fatigue, thereby improving exercise 109 tolerance. To our knowledge, this has yet to be evaluated directly.

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### 111 [insert figure here]

112

Figure 1. Putative mechanisms underlying improved respiratory muscle function and
exercise performance following "standalone" inspiratory muscles training (IMT). (?)
indicates that this mechanism is yet to be investigation.

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## 117 Does inspiratory loading during exercise have an ergogenic effect?

Finally, we close by considering how knowledge of putative mechanisms described above should influence the way in which IMT is implemented in practice; specifically, is there any rationale for loading to be applied during exercise?

121 A recent systematic review (17) of nineteen studies concluded that inspiratory 122 loading during AE impairs exercise tolerance due to an inadequate ventilatory  $(V_E)$ 123 response. Amongst the twelve studies that reported peripheral oxygen saturation (SpO<sub>2</sub>), 124 seven showed a decrease in  $SpO_2$ . On the other hand, when inspiratory loading was 125 applied during recovery from high-intensity interval training, a positive effect was 126 found upon clearance of lactate. The psychophysiological effects of imposing 127 respiratory loads during exercise are negative and well-established (17), including 128 increased breathing discomfort, anxiety and intensification of effort during AE.

Accordingly, we argue that imposing an ergogenic intervention, such as inspiratory loading, *during* exercise has the same pitfalls as training at high altitude; specifically, it impairs the quality of the training that can be accomplished, whilst not providing any additional benefits to sea-level performance (18). Altitude researchers realised quickly that the benefits of altitude training could be optimised by adopting the so-called 'live-high-train-low' paradigm, whereby the erythropoietic benefits of altitude exposure were achieved without compromising athletes' training quality (18). Our understanding of the mechanisms that underpin the ergogenic effects of RMT (see figure 1), as well as the conclusions of the systematic review by López-Pérez (17), lead to the inevitable conclusion that implementing RMT via respiratory loading *during* AE sessions is a mistake. Moreover, this combination may lead to harmful psychophysiological effects, whilst also being ineffective (17). In contrast, there is ample evidence that the implementation of "standalone" IMT using resistance-training principles is well-tolerated and highly effective for a wide range of individuals (19).

143 The results of RCTs suggest that IMT is a key part of exercise-based cardiac and 144 pulmonary rehabilitation programs. However, in these studies, IMT protocols were conducted in separate sessions, and they provided benefits in cardiorespiratory 145 responses to exercise and reduced dyspnoea in CHF (9) and COPD patients (10), 146 respectively. Based on the current literature, it is recommended to combine IMT with 147 148 AE in separate sessions. In summary, using inspiratory loading during AE may have a negative impact, whereas performing IMT and AE in separate sessions allows for 149 sufficient recovery and may lead to additional physiological enhancements compared to 150 151 just doing IMT or AE training alone.

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#### **153** Conclusions and future directions

154 Finally, there is one context in which we recommend further research into the 155 effects of combining RMT with other forms exercise. A single study has investigated 156 the combination of IMT with whole body, "functional" strength training (19). The data 157 suggested that a standalone IMT provided a foundation of improved inspiratory muscle strength and core muscle functions. Furthermore, a follow-on programme of IMT, 158 159 combined with simultaneous core muscle training exercises, enhanced core muscle 160 function further, as well as and providing cumulative benefits to running performance. 161 The mechanistic rationale for this approach is the role of the respiratory musculature in 162 trunk stabilisation (2), as well as in balance (20). To underscore, a strong foundation of standalone IMT was the first step of the aforementioned study and, in our opinion, is 163 164 crucial to support the combination of IMT with other forms of strength training.

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Mechanism 1: *Respiratory muscle metaboreflex* (5, 13)

Mechanism 3: *Reduced oxygen cost of breathing* (16)

Improved respiratory muscle function and exercise performance following IMT Mechanism 2: *Reduced effort perceptions* (4, 14)

Mechanism 4: *Attenuation of central fatigue* (potential mechanism?)

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