EXERCISE, SPORTS AND TRAINING AT HIGH ALTITUDE

EXERCISE TRAINING AT HIGH ALTITUDE: HOW DO THE RESPIRATORY MUSCLES RESPOND?

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RESUMEN: Ejercicios de entrenamiento en altura: Cómo responden los músculos respiratorios?

Al igual que todos los músculos esqueléticos de vertebrados, los músculos ventilatorios (VM) de humanos pueden mejorar adaptativamnete en su capacidad funcional. Puesto que estos cambios ocurren consistentemente en respuesta a protocolos específicos de entrenamiento de resistencia y fuerza para los VM, se podría asumir que se aplican los mismos principios de entrenamiento de músculos esqueléticos a los músculos ventilatorios. Sin embargo, es aparente que las adaptaciones de los VM requieren ejercicios muy fuertes (y tal vez un tipo de entrenamiento específico), puesto que el ejercicio de entrenamiento crónico de animales totales no parece tener un efecto significativo o siquiera predecible sobre los aspectos estructurales o funcionales de los VM. En este artículo se revisa los resultados ambiguos de varios programas de ejercicio de entrenamiento regular con respecto a los músculos respiratorios de animales. También se revisa estudios de entrenamiento de altura, dirigidos a incrementar la fuerza de estímulo necesario para las adaptaciones de los VM, estudios que tampoco revelan cambios funcionales de los VM. Finalmente, puesto que parece haber una relación pobre entre poder de los VM y entrenamiento incluso con incremento de altitud, se plantea la pregunta de si el diseño evolutivo de los VM es primariamente para "respiración". Proponemos una hipótesis alternativa, que la ventilación no ha sido seleccionada como la tarea primaria de los VM. Más bien, son tareas no ventilatorias las que plantean una mayor demanda que la ventilación misma sobre los "músculos ventilatorios".

Palabras claves: Entrenamiento de resistencia, Altitud, Plasticidad muscular

RÉSUMÉ: Exercices d'entraînement à grande altitude : Comment répondent les muscles respiratoires?

Comme tous les muscles squelettiques des vertébrés, les muscles de la ventilation respiratoire (VM) des humains peuvent s'adapter et améliorer ainsi leur capacité fonctionnelle. Ces changements survenant invariablement en réponse à des protocoles spécifiques d'entraînement de force et d'endurance des VM, on pourrait penser que les mêmes principes d'entraînement des muscles squelettiques s'appliquent aux muscles respiratoires. Cependant, il apparaît que les adaptations des VM nécessitent des exercices de stimulation très intenses (et peut-être un type d'entraînement spécifique), étant donné que l'exercice d'endurance prolongé des animaux vivants ne semble pas avoir d'effet significatif ni même prévisible sur les aspects structuraux ou fonctionnels des VM. Dans cet article ont été révisés les résultats ambigus de plusieurs programmes d'exercice régulier d'endurance concernant les muscles respiratoires d'animaux. De même ont été reconsidérées les études d'entraînement à l'endurance à grande altitude visant à augmenter la force du stimulus nécessaire aux adaptations des VM, études qui ne révèlent pas davantage de changements fonctionnels des VM. Finalement, puisqu'il ne semble y avoir qu'un faible rapport entre puissance des VM et endurance, même lorsque l'altitude augmente, on se pose la question de savoir si les VM ont été conçus en premier lieu pour la "respiration". Nous proposons une autre hypothèse : que la ventilation respiratoire n'a pas été sélectionnée comme étant la tâche primordiale des VM et que ce sont au contraire les tâches non respiratoires, plus que la respiration en elle-même, qui exigent davantage des "muscles respiratoires".

Mots-clés : Entraînement d'endurance, Altitude, Plasticité musculaire.

SUMMARY: La Stayo et al.: Exercise training at high altitude: how do the respiratory muscles respond?

Like all vertebrate skeletal muscles, the ventilatory muscles (VM) of humans can adaptively improve in their functional capacities. Since these changes occur consistently in response to specific VM strenght and endurance training protocols, one would assume the same principles of skeletal muscle training can be applied to the VM. It is apparent, however, that VM adaptations require a very strong exercise stimulus (and perhaps a VM training specific stimulus) as chronic whole animal endurance exercise do not appear to have significant or even predictable effect effect on the structural or functional aspects of the VM. This manuscript reviews the equivocal results regarding animals' respiratory muscles to various programs of regular endurance exercise. It also reviews endurance training studies at high altitude, predicted to increase the strenght of the stimulus for VM adaptations, which again fails to elicit VM

functional changes. Finally, since there seems to be a poor relationship between VM power and endurance with increases in (even at altitude) the question is raised as to whether the evolutionary design of the VM is primarily for "breathing". We propose an alternative hypothesis that ventilation has not been selected as the primary task of the VM. Rather, non-breathing tasks put a larger demand on the "ventilatory muscles" than does ventilation per se.

Key words: Endurance training, Altitude, Muscle plasticity

INTRODUCTION

Like all vertebrate skeletal muscles, the ventilatory muscles (VM) of humans can adaptively improve in their functional capacities. These changes occur consistently in response to specific VM strength and endurance training protocols. There is less evidence, however, that functional or structural adaptations occur as a consequence of increased ventilatory demands concomitant with whole animal, i.e., chronic endurance training. Even when the magnitude of the challenge to the VM is increased dramatically, as with endurance training at altitude, there may be adequate VM functional capacity to meet this demand. Therefore, the question remains as to what type and magnitude of whole animal chronic endurance training would produce a phenotypic shift in the VM similar to that seen in skeletal muscle exposed to similar stressors. That is, since chronic endurance training combined with high altitude conditions is a strong stimulus for adaptive skeletal muscle changes (see papers in this issue), yet VM remains unchanged, what stressors are needed for VM to adaptively respond ?.

SKELETAL MUSCLE PLASTICITY

Virtually every structural aspect of muscle can change given the appropriate stimulus. In general, these transformations have been documented in a number of different muscles and species and include (but are not limited to) changes to architecture (1,2), fiber type (3-5), mitochondrial distribution, capillary density (6), etc.

Functional changes are causally linked to these structural changes (7). For instance, the capillary density and mitochondrial content increase in response to chronic whole body endurance training as does VO_2max (6). The adaptive response of skeletal muscle may be even greater in magnitude when training is performed at altitude (8,9). Studies using muscle biopsies have shown that endurance exercise performed at high altitude can affect muscle structure. Desplanches et al (10) compared 3 weeks (2 hr/day) of cycle ergometry exercise in subjects who first trained in severe hypoxia (5500 m) and then 14 months later trained in normoxia. The effect of high altitude significantly increased the average muscle fiber area, capillary to fiber ratio and total mitochondrial volume, but the same level of training at sea level produced no significant morphometric changes. Citrate synthase also has been shown to significantly increases in muscles trained in hypoxia (2300 m) as compared to muscles trained in a normoxic setting (11).

ARE THE VENTILATORY MUSCLES PLASTIC ?

If the VM share the same phenotypic plasticity as other skeletal muscle, chronic exposure to an exercise bout which results in significant muscle loading should be a powerful stimulus for the production of specific functional as well as structural adaptations to occur. Therefore, one might expect some structural and functional adaptations to the VM with endurance type exercise. Regarding VM, however, chronic whole animal endurance exercise (even in hypoxic settings) does not appear to have a significant or even predictable effect on the structural or functional aspects of the VM. Numerous investigators have examined the adaptive responses of animals' respiratory muscles to various programs of regular endurance exercise, however, the results are equivocal. Guinea pigs trained by endurance running for 6 weeks showed no significant effect on muscle mitochondrial content and capillarity in the diaphragm (12). Likewise, a number of earlier studies failed at demonstrating training effects on the diaphragm induced by whole body exercise (13-15). Several reports, however, demonstrate increases in the activity of marker enzymes of oxidative metabolism in the diaphragm of rats subjected to various types of endurance training (16-20). Powers et al. (16-19) and Uribe et al. (20) have reported increases in aerobic marker enzymes in the rat diaphragm following various intensities of chronic endurance training. Taken collectively, these animal studies demonstrate some functional phenotypic plasticity of the ventilatory muscles. It has been hypothesized, however, that exercise intensity must be very high indeed to induce structural adaptations in the diaphragm (16,19,20).

Some studies on humans suggest that VM endurance can be improved with swimming or running exercises (21,22). Following three

months of swim training, Clanton et al (22) observed a significant increase in inspiratory muscle endurance nearly equal to that observed in a group of swimmers who underwent the same swim training, but in addition performed inspiratory muscle training. Likewise, Robinson and Kjeldgaard (21) linked a 16% increase in ventilatory muscle endurance to a similar increase in running performance following training in a group of previously sedentary humans. Neither of these studies reported VO_2max before and after training. Moreover, swimmers' specialty (sprint versus endurance) were not reported making it difficult to judge the magnitude of the training effect. Therefore, swim- or run-training performed at sufficient intensities may improve the structural and functional capacity of the chest wall muscles. The possible explanation for an adaptive effect with human swimming, and in the quadruped/animal treadmill running regimes, is that the chest wall muscles (which includes to some degree the VM) are recruited for propulsion, not just ventilation. Although bipedal running does not recruit the chest wall musculature to the same degree, it is conceivable that substantial running efforts (as may be seen in previously sedentary subjects who are submitted to a novel running program) may involve ample upper extremity movement so as to stimulate the VM more than when the VM are used solely for ventilation.

It is apparent that some modes of endurance exercise can formidably stress the VM. Coast and Weise (23) reported a significant decrease in MIP at the mouth following a progressive load cycle ergometry test to exhaustion. In the same study, however, following the VO_2max test, a group of elite cross-country skiers (mean VO_2max = 71.8 ± 3.8 mlO_2 kgl min^{-1}) "protected" their MIP. During a competitive classical triathlon, Hill et al (24) observed a non-significant decline in maximum inspiratory pressure measured at the mouth following the swim leg and a significant decrease in MIP following the bike and run legs respectively. Loke et al. (25) also measured a 16 % decrease in MIP in four subjects after completing a marathon. From these studies it seems that the parameters setting MIP are malleable as a function of certain types of repetitive exercise stress, but the effects appear to be mode and intensity of exercise specific.

In contrast to whole-body endurance training, specific respiratory tasks that emphasize both VM strength and endurance unambiguously provide a powerful stimulus sufficient to induce adaptive changes. In the laboratory, specific VM training protocols have resulted in significant improvements in ventilatory capacity tasks (26-29). In a now classic study, Leith and Bradley (26) studied respiratory mechanics before and after a 5 week training program that included maximum static inspiratory and expiratory maneuvers and "ventilating to exhaustion" 30-45 minutes/day, 5 days /week. In applying accepted principles of skeletal muscle training to the VM (and seeing significant improvements in VM strength and endurance) it has been concluded that appropriate VM training programs can promote adaptive changes.

It is apparent that VM adaptations require a very strong exercise stimulus (and perhaps a VM training specific stimulus). The reason for this may be that the main VM muscle, the diaphragm, is extremely well equipped to perform continuous work and very specific high intensity exercises are needed to induce changes. The mitochondrial content and capillary supply of the diaphragm, in a considerable number of mammalian species analyzed, consistently surpasses that of locomotor muscles (diaphragm being second only to the heart with respect to these characteristics; (30,31). Some would suggest that VM structure is "overbuilt" for breathing tasks and does not contribute to limiting aerobic performance in chronic whole body endurance activities (32). That is, are the VM of animals built with a fundamental balance between structure and function and do they uphold the concept of optimal design, or symmorphosis (33).

THE CONTRIBUTION OF THE VENTILATORY MUSCLES TO AEROBIC PERFORMANCE AT ALTITUDE

Since aerobic performance and VO_2max at altitude are primarily constrained by availability of environmental oxygen (34,35) one would expect the stressors on the VM to be greater at altitude and hence provide an ideal stimulus for VM adaptive changes to occur. This hypothesis was tested in human subjects (at a moderately high altitude) by examining peak inspiratory flow and its contribution to oxygen demand (36). In this study peak inspiratory flow performance was compared between trained (Vo_2max> 65 ml O_2 kg~l min^{-1}) and untrained (VO_2max< 45 ml O_2 kg^{-1} min^{-1}) subjects, at a moderately high altitude (2100 m). Despite great differences in Vo2max and exercise habits and abilities between the two groups of subjects, their respective inspiratory muscle performances were indistinguishable (figure 1). Consequently, there was no evidence

that regular and high-intensity chronic whole body endurance training at moderate altitude elicits adaptations of either airways or inspiratory muscles. It is as interesting to note that when the data from the trained and untrained subjects are extrapolated, the inspiratory capacities of these subjects (even without any adaptation) could potentially support ventilation sufficient for a Vo2max of 85 ml O_2 kg^{-1} min^{-1}, which is the highest recorded value in humans (37). Therefore, the VM would seem to be "overbuilt" in most individuals, with only those of very rare elite endurance athletes conforming to the concept of ' symmorphosis.'

Obviously the VM stressors need to be very high for potential adaptations to occur with endurance exercise.

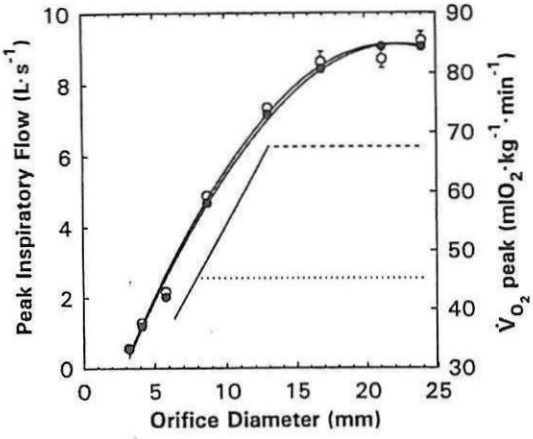

Figure 1. Highly trained cyclists, VO_2max = 68 ml O_2 kg^{-1} min^{-1} (filled symbols) and their sedentary controls, VO_2max = 45 ml O_2 kg^{-1} min^{-1} (open symbols) have nearly identical peak flows when breathing through inspiratory resistors. However, when the two groups of subjects are asked to cycle at workloads corresponding to their respective VO_2max both can do so while breathing through a resistor that caused a reduction in peak flow (trained: dashed line; sedentary, dotted line). Further, the sedentary subjects can maintain their Vo2max while breathing through much smaller orifices (#8mm) than can the trained subiects (≈13mm). In all subiects, peak Vos declined as a function of smaller orifice diameters, indicating peak VO_2 was ventilation limited. When this regression line is extrapolated, it predicts that the inspiratory resistor necessary to cause a decline in peak flow, would result in a decrease in Vo_2 only if VO_{2max} exceeded 85 ml O_2 kg^{-1} $.min^{-1}$, nearly equal to the highest usually reported in humans. (From 32. Used with permission from Respiratory Physiology).

Since VM adaptations did not occur with endurance exercise at moderate altitude, one way of increasing the VM demand greatly is to train at an even higher altitude, thereby providing a more powerful ventilatory challenge and critical test of VM functional plasticity in humans. Therefore, we measured VM power and endurance in a group of high altitude residents of La Paz, Bolivia (3600 m) prior to and immediately following an endurance training protocol designed to increase Vo_2max (see Favier et al., 1995b). Specifically, we tested the hypothesis that the static (isometric) and dynamic (miometric) properties of the human ventilatory muscles, as defined by the slope of the maximum inspiratory pressure-flow curve (MIPF) through graded resistors, the maximum sustainable ventilatory capacity (MSVC) and the maximum 12 seconds ventilation (MVV_{12}) will respond adaptively to six weeks of hypoxic endurance (cycle ergometry) training.

A group of 18 young men, residents of La Paz, Bolivia (3600m) were assigned to either an endurance training (ET) or control (C) group. The endurance training program consisted of cycling for 30 min/day, 5 day/wk, for 6 wk at an external power output initially set to elicit 70 % of their individual VO_2max. Our hypothesis predicted that endurance training at high altitude should provoke detectable functional adaptations of the ventilatory muscles. However, this study failed to demonstrate this result. Peak inspiratory pressures, flows, MVV_{12} and MSVC, were not different before vs. after nor comparing post-training values with those of control, untrained, subjects (figure 2).

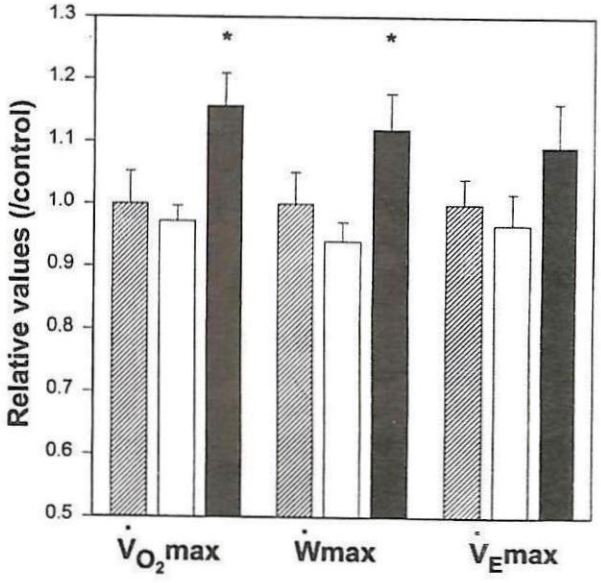

Figure 2. When healthy, but untrained, subjects trained on the cycle ergometer at 3,400 meters in

La Paz, Bolivia, they experienced a significant increase in VO_2max, and the maximum workload (Wmax) comparing before training (empty bars) with after training (filled bars), while maximum ventilation ($V_E$max) increased insignificantly. Untrained control subiects are shown in hatched bars.

Despite the fact that VO_2max did significantly increase, that increase was not accompanied by significant changes in either $V_E$max, nor in any of our measures of ventilatory muscle performance. Thus, these results suggest accepting the null hypothesis that VM power and endurance do not track increases in VO_2max in humans, even when exercise training is carried out in environmental hypobaric hypoxia. These results coincide with another study which assessed the effect endurance training at altitude on maximal inspiratory pressure (38). Like the results in the Bolivia study, VO_2max increased after training, but the maximal inspiratory pressure and inspiratory muscle fatigue did not. From these studies, which theoretically increased the stimulus for VM muscle adaptation via a hypoxic condition, we have to conclude that sufficient VM structural and functional capacity was present prior to the endurance training bout to accommodate increases in VO2max. In other words, this implies that the inspiratory muscles do not limit performance and there apparently is "excess ventilatory muscle architecture" in all but the most elite endurance athletes.

ARE THE VENTILATORY MUSCLES PRIMARILY FOR VENTILATION?: AN ALTERNATIVE HYPOTHESIS

There seems to be a poor relationship between VM power and endurance with VO_{2max} suggesting that the evolutionary design constraints for these muscles may not be the breathing task (40). As an alternative hypothesis, we have proposed that ventilation, even maximum sustainable ventilation, has not been selected as the primary task of the VM. If non-breathing tasks (e.g. trunk tasks such as lifting, coughing, yawning, sneezing, or posture) put a larger demand on (i.e., require greater recruitment of) the 'ventilatory muscles' than does ventilation (even during hyperpnea of exercise in hypoxia), these tasks should promote measurable changes in VM capacity.

To test this alternative hypothesis, that the VM respond primarily to non-respiratory tasks such as upper body exertion, we measured inspiratory power and maximum ventilation in 6 healthy young males prior to and immediately following a 6 week training program (consisting of working with free weight and calisthenics) (41). Resistance exercises were designed to work on the trunk muscles without increasing ventilation. Four subjects did no training and functioned as controls. Subjects in the trained group experienced an increase in VM inspiratory power, as determined by pressure-flow curves, and the VM capacity both acutely (MVV12, 12% increase, p=0.0014) as well as MSMV (12% increase, p=0.0023) (figure 3). These preliminary results suggest that the ventilatory muscles are very responsive to non-respiratory tasks, more so than to the normal ventilatory demands of chronic whole animal endurance exercise.

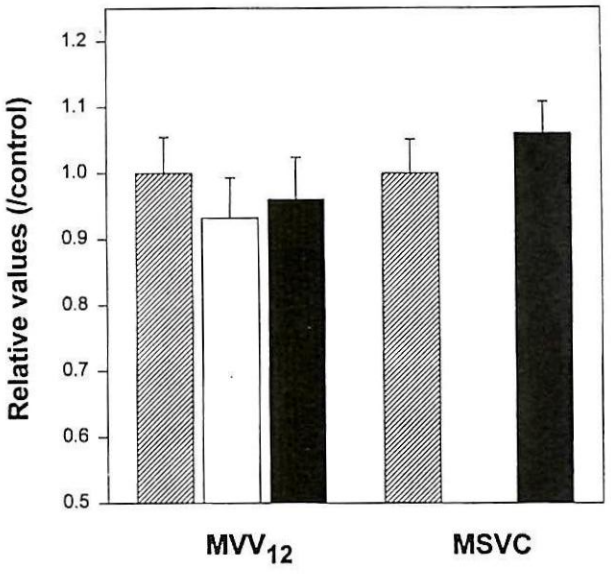

Figure 3. Despite significant increases in VO_2max and work output, training for 6 weeks at 3,400 meters had no significant effect on maximum voluntary ventilation in 12s (MVV_{12}) nor on the maximum sustained ventilatory capacity (MSVC). (These data are from 36).

The fact that ventilatory parameters do not predictably change with chronic, whole animal endurance training (even in severe hypoxic settings) may be evidence that this type of training is quite variable. As well, the stressors to the VM are not consistently adequate enough to promote VM changes with endurance training. This, coupled with an apparent excess of VM structure, suggests specific, high-intensity VM stressors are needed to produce a phenotypic shift in the VM. Certainly, VM specific exercises (like inspiratory and expiratory maneuvers and ventilating to exhaustion over a 5 week training period) provide ample stimulation, but perhaps non-respiratory tasks (such as upper body resistance exercises) can also be considered when attempting to

adaptively improve the functional capacity of the VM. Acknowledgments: This work was supported by NSF IBN 17527 and NIH - MBRS GM 821510 to SLL. We are grateful for the collaborative support and lucid insights of David Leith and for continued support from Hanz Hoppeler.

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