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PERSPECTIVES

Exercise and the lungs: nature or nurture?

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The lungs are a component of the respiratory system, which also includes the oral/nasal passages, trachea and muscles of respiration. With the exception of the diaphragm and the other muscles supporting respiration, the respiratory system has long been viewed as untrainable in response to exercise. Indeed, unlike the cardiac and skeletal muscle, which can undergo structural and morphological changes to improve their function with exercise training, lung structure is not found to change with training, resulting in minimal (if any) changes in lung volume or function.

This lack of plasticity is generally not a problem, as most healthy individuals performing exercise (at or near sea level) are able to maintain normal arterial oxygen levels, even during maximal exercise. Moreover the lung, and more generally the respiratory system, is often found to provide unfailing support for gas exchange under peak demand (e.g. during maximal exercise) in healthy mammals, and therefore it has widely been accepted that the lungs are 'overbuilt' for their primary gas exchange function. A notable exception applies to highly fit or elite-level athletes, who can experience gas exchange impairment particularly as exercise intensity approaches peak aerobic capacity, resulting in a phenomenon known as exercise-induced arterial hypoxaemia (EIAH). This is not unique to humans, as other mammals with high aerobic capacity (horses, dogs, etc.) are also found to exhibit EIAH (Dempsey & Wagner 1999). The physiological mechanisms that underpin hypoxaemia can be narrowed to one or more of the following: inadequate ventilation, mismatching of ventilation and perfusion in the lung, shunting of venous blood to the arterial side (i.e. bypassing gas exchange), and diffusion limitation. While these are well established, the relative contribution from any of these specific mechanism(s) in the aetiology of EIAH is still the focus of investigation. This is, in part, because EIAH is not a universal finding among athletes, and is even found in individuals (typically women) with $\dot{V}_{O_2max}$ much lower than the frequently reported threshold of 60 ml kg^{-1} min^{-1} that is often associated with EIAH (Harms *et al.* 1998). Clinicians and scientists are left wondering why, and whether some component of lung structure (if not changing) may respond differently to exercise training, between athletes, between aerobically fit *versus* unfit individuals, or between the sexes.

In a recent study, Lalande *et al.* (2012) reported that individuals with high $\dot{V}_{O_2max}$ were found to have greater pulmonary capillary blood volume at rest, questioning if aerobically fit individuals have a more distensible pulmonary circulation. In a recent issue of *The Journal of Physiology*, Tedjasaputra *et al.* (2016) have further explored this finding and ask the next logical question, does greater fitness level alter lung diffusing capacity (DLCO) at or near maximal exercise? And if so, do these changes occur via pulmonary capillary blood volume (V_c) and/or with changes in diffusion across the alveolar membrane (D_m)? While this is not the first study to attempt to measure DLCO during exercise, the ability to measure DLCO near maximal exercise is extremely challenging since the subject is required to perform a breath-hold. It is notable that the investigators were able to obtain high-quality data on DLCO at exercise workloads of 90% of $\dot{V}_{O_2max}$, when the lungs and gas exchange are close to the greatest stress and demands. Their study reveals that DLCO was greater in subjects with high aerobic capacity (HI-Fit group with $>$ 60 ml kg^{-1} min^{-1}) compared with individuals with lower aerobic capacity (LO-Fit group with $\sim$45 ml kg^{-1} min^{-1}), and this was due to an increase in the D_m component and not V_c. These data suggest that endurance trained athletes have a larger alveolar–capillary interface, which is advantageous for the transfer of O_2 during intense exercise. Although the current study does not directly address the issue of EIAH, and it is not stated in the report whether EIAH even existed in any of the subjects, these data establish that there are differences in the lung diffusing capacity between highly fit *vs.* less aerobically fit individuals. This raises a number of interesting questions: (1) have the lungs in these high-level endurance athletes changed with training to allow for this advantage? Or (2) is the ability of individuals to achieve high levels of lung and aerobic performance genetically pre-selected (i.e. nature *vs.* nurture)? And, (3) do the lungs in some people respond differently from in others, perhaps contributing to the variability between those who experience *vs.* those that don't experience EIAH?

Based on the evidence currently available in the literature, it seems unlikely that DLCO changes significantly with training (Flaherty *et al.* 2014). It is also notable, however, that lung size of the HI-Fit group was greater than the LO-Fit group in Tedjasaputra *et al.*'s paper, suggesting the answer for diffusion may rely on 'nature' rather than 'nurture'. This conforms to the notion that lung size (which is genetically determined) is likely to be an important factor determining whether an athlete will experience EIAH. Conceptually, it seems logical to expect that individuals with a small stature (and therefore small lungs) and who also achieve/develop a high aerobic capacity (via training) may be predisposed to EIAH. This is consistent with the observations found in exercising women (who on average have smaller lungs compared with similar stature males) are found to be more susceptible to EIAH (Harms *et al.* 1998). Interestingly, when highly fit women are matched to males based on lung size, they do not appear to be more susceptible to EIAH (Olfert *et al.* 2004). Therefore, although EIAH is most commonly observed in athletes with high $\dot{V}_{O_2max}$, it should be the combination of lung size and how strongly the aerobic/metabolic engine is developed by training in any individual (i.e. establishing the demand on the lung) that determines whether gas exchange impairment and EIAH occur. Practically speaking, EIAH is unlikely to occur in individuals with low aerobic fitness, because even the smallest of healthy lungs appear to be more than adequate to meet the

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peak aerobic demands with this phenotype. However, as aerobic fitness and demand increase, lung size (and therefore D_m) becomes increasing important, such that individuals with smaller lungs and high aerobic demand are likely to be the most susceptible to EIAH. Thus, in principle, any person may experience EIAH if he or she develops an aerobic demand that exceeds supply for the supply and demand relationship that exists for total transfer of oxygen across the alveolar membrane at or near peak aerobic demand. So it seems the combined effect of 'nature' and 'nurture' must both be considered in determining the effect of the lung during exercise.

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