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The effects of smoking and hypoxia on skeletal muscle structure and function

Wust, R.C.I.

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Abstract

Chronic obstructive pulmonary disease (COPD) is increasingly common and in 80% of the patients it is caused by cigarette smoking, often over several decades. Exercise intolerance is a major problem in COPD and there is accumulating evidence that this is not solely due to reduced lung function but that it also involves skeletal muscle. It is not known if changes in skeletal muscle tissue occur before clinical symptoms of COPD are apparent. Therefore the main aim of the work described in this thesis was to gain insight into the extent to which cigarette smoking and hypoxaemia affect the functional and morphological changes of skeletal muscle.

Percutaneous electrical stimulation of the quadriceps muscle (2 minutes 30 Hz with duty cycle of 0.5; 1 s on, 1 s off) was used to assess fatigue characteristics to avoid possible problems of differences in voluntary activation.

In non-smoking participants, women were generally more fatigue-resistant than men. Young men with a relatively short smoking history were more susceptible to fatigue than non-smoking, age- and physical activity-matched peers. In a larger cohort of smokers spanning a wide range of age and smoking history, it appeared that this lower fatigue resistance was not related to smoking history. The similar contractile speed in smokers and non-smokers suggests that factors other than differences in muscle fibre composition underlie the reduced fatigue resistance in smokers. The reduced fatigue resistance might be more related to a possible acute, and possibly reversible, impairment of smoking on the oxygen supply or the ability to use oxygen for aerobic energy generation by the muscle.

Subsequently, the effects of chronic hypoxia on determinants of oxygen supply and oxidative capacity were studied. Adaptations within the rat plantaris muscle to chronic hypoxia were region- rather than fibre type-specific. Hypoxia resulted in atrophy in all regions of the muscle. However, capillary proliferation only occurred in the deep, oxidative region, and mitochondrial biogenesis was restricted to the superficial, glycolytic region. Model calculations indicate that these adaptations to hypoxia prevent the occurrence of anoxic areas in the deep region, but that in superficial regions tissue oxygenation becomes more problematical during hypoxia. These results are discussed in relation to their possible relevance in understanding muscle function in COPD patients.