Training intensity-dependent regulation of mitochondrial respiration in human skeletal muscle: an effect modulated by the transcription factors PGC-1α, p53 and PHF20

C. Granata,[1] R.S.F. Oliveira,[1] K. Renner,[2] J.P. Little[3] and D.J. Bishop,[1] [1]Institute of Sport, Exercise and Active Living (ISEAL), Victoria University, Melbourne, VIC 3031, Australia, [2]Department of Hematology and Oncology, University Hospital Regensburg, Germany and [3]School of Health and Exercise Sciences, Faculty of Health and Social Development, University of British Columbia Okanagan, Kelowna, BC V1V 1V7, Canada.

Mitochondria are key components of skeletal muscles as they provide the energy required for almost all cellular activities, and play an important role in ageing and cell pathology. Exercise training at different intensities has been shown to enhance mitochondrial biogenesis and improve endurance performance. However, the role of training intensity on mitochondrial respiration has not been defined. Moreover, recent studies have reported that mitochondrial respiration is a more important determinant of endurance performance than mitochondrial content (Jacobs *et al.*, 2011). Therefore our purpose was to compare the effects of 4 weeks (12 sessions) of sub-lactate threshold continuous training (STCT), high-intensity interval training (HIT) and sprint interval training (SIT) on mitochondrial respiration in permeabilised muscle fibres, and on markers of mitochondrial biogenesis in human skeletal muscle. We also aimed to determine if changes in mitochondrial respiration were related with changes in 20 km cycling time trial (20k-TT) performance. We hypothesized that mitochondrial respiration, and the protein content of transcription factors involved in the regulation of mitochondrial biogenesis, would be increased in an intensity-dependent manner, and that changes in mitochondrial respiration would be associated with changes in endurance perfomance.

Twenty-nine active men (21 ± 2 y, 46 ± 6 mL O_2 min^{-1} kg^{-1}) were matched for the power attained at their lactate threshold (W_{LT}) obtained during a graded exercise test (GXT), and assigned to either the STCT (20-36 min at 90-97.5% W_{LT}; n = 9), HIT (4-7 x 4 min at W_{LT} + 35-75% [W_{Peak} - W_{LT}], with W_{Peak} representing the peak power obtained during the GXT; n = 11) or SIT (4-10 × 30-s “all-out”; n = 9). Resting muscle biopsies (*vastus lateralis*) were obtained at baseline, and 72 h after the last training session. Maximal ADP-stimulated mitochondrial respiration (V_{max}) increased by 25 ± 20%, following SIT ($P < 0.05$), but not STCT or HIT (both $P > 0.05$). Similarly, the protein content of peroxisome proliferator-activated receptor γ coactivator-1α (PGC-1α), p53, and plant homeodomain finger-containing protein 20 (PHF20), three transcription factors involved in the regulation of mitochondrial biogenesis, was significantly increased (~60-90%) following SIT (all $P < 0.05$), but not STCT or HIT (both $P > 0.05$). Citrate synthase (CS) activity, a common biomarker of mitochondrial content, and the protein content of mitochondrial transcription factor A (TFAM), an important mitochondrial transcription factor, did not change significantly following either of the 3 protocols (all $P > 0.05$). Finally, 20k-TT performance was improved following STCT and HIT (~5%, both $P < 0.05$), but did not change following SIT ($P > 0.05$). Our findings demonstrate that training intensity is a key factor regulating mitochondrial respiration, and indicate a dissociation between training-induced changes in mitochondrial respiration and content. We also provide evidence that changes in mitochondrial respiration, but not mitochondrial content were associated with changes in the protein content of PGC-1α, p53 and PHF20. Finally, our research shows that changes in endurance performance were not correlated with changes in mitochondrial respiration, suggesting that mitochondrial respiration is not the key mediator of changes in endurance performance in active individuals.

Jacobs RA, Rasmussen P, Siebenmann C, Díaz V, Gassmann M, Pesta D, Gnaiger E, Nordsborg NB, Robach P & Lundby C. (2011). Determinants of time trial performance and maximal incremental exercise in highly trained endurance athletes. *Journal of Applied Physiology* **111,** 1422-1430.