Skeletal muscle mitochondrial function and ROS production in response to extreme endurance exercise in athletes.

Maria Fernström [1,2], Irina Shabalina [2,5], Linda Bakkman [1,2], Michail Tonkonogi [4] Mikael C. Mattsson [2], Jonas K.Enqvist [2], Björn Ekblom [2] and Kent Sahlin [2,3]

1. Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden. 2. Stockholm University College of P.E. and Sports, GIH, Stockholm, Sweden. 3. Institute of Sport Sciences and Clinical Biomechanics, University of Southern Denmark, Odense, Denmark. 4. University of Dalarna, Falun, Sweden. 5. The Wenner-Gren Institute, Stockholm University, Stockholm, Sweden.

Although it is well known that endurance exercise induces oxidative stress (1) there is no evidence of deteriorated mitochondrial function after 1-2 hours intensive exercise (2). However, the effects of extreme endurance exercise on mitochondrial function and mitochondrial ROS production have not been investigated previously.

Nine healthy well-trained men (age 27.1 ± 0.87 (mean ± SE), BMI 24.2 ± 0.64 and VO_2 peak 62.5 ± 1.78 ml/kg. min) performed 24 hours exercise, consisting of equal parts running, cycling and paddling. Muscle biopsies were taken from vastus lateralis pre-exercise (PreEx), immediately post-exercise (PostEx) and after 28 hours of recovery (PostEx-28). Mitochondria were isolated and mitochondrial respiration was analyzed with palmitoyl-carnitine (PC) and pyruvate (Pyr). Mitochondrial H_2O_2 release was measured with the Amplex Red-horseradish peroxide method. The reaction was initiated by addition of succinate with following addition of antimycin A (reversed electron flow).

UCP3 protein expression, evaluated with western blot technique, was not changed by exercise. Both state 3 (Pyr and PC) and state 4 (PC) rates of oxygen consumption (estimated per maximal ETC-activity) were increased PostEx (+29%, +11% and +18%). State 3 remained elevated PostEx-28, whereas state 4 (Pyr) decreased below that at PreEx (-18%). Mitochondrial efficiency (P/O) decreased PostEx (Pyr -8.9%, PC -6.1%) and remained reduced PostEx-28. The relative substrate oxidation (state 3 PC/Pyr) increased after exercise PreEx: (0.71 ± 0.06 vs. PostEx (0.90 ±0.04) and (0.77 ±0.06) PostEx-28. Mitochondrial H_2O_2 release (succinate) increased dramatically after exercise (+189 ± 64%). Treatment with Antimycin A resulted in a twofold-increased rate of mitochondrial H_2O_2 release PreEx but a decreased rate in PostEx samples. The exercise-induced changes in mitochondrial ROS production was totally abolished PostEx-28.

In conclusion extreme endurance exercise decreases mitochondrial efficiency and increases mitochondrial ROS production. Both of these changes would increase the oxygen demand during exercise. Relative fatty acid oxidation as measured in isolated mitochondria increased after exercise indicating that the capacity to oxidize fat is improved during prolonged exercise.

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2. Tonkonogi, M., et al., *Mitochondrial function and antioxidative defence in human muscle: effects of endurance training and oxidative stress.* J Physiol, 2000. **528 Pt 2**: p. 379-88.