# Aerobic exercise training in temperate or hot environments similarly improves performance and induces a fast to slow fiber type shift

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**Introduction:** Heat (H; ≥32°C) stress acutely worsens aerobic performance. However, H has emerged as a potential therapy to modulate muscle metabolism inducing aerobic phenotype and it is unknown the effects of training in this condition for long periods (> 4weeks) on muscle fiber type and trophism and intracellular pathways regulating muscle phenotype. **Objective:** To evaluate the morphological, metabolic and molecular adaptations in skeletal muscle induced by long-term aerobic physical training (APT) in H. **Methods:** Adult, male Swiss mice (40g) were divided in: 1) Sedentary (SED) mice kept in the temperate (T) environment (22°C;SED/T), 2) SED kept in H (32°C;SED/H), 3) mice trained (TRA) in treadmill (1h/day, 5days/week, 8weeks, 60% of maximum speed (Smax)) in T (TRA/T), and 4) TRA in H (TRA/H). All groups performed incremental load tests in T and H before (pre-training) and after 4 and 8 weeks of training. The liver and muscle glycogen content were measured by Anthrone method and mitochondrial activity. Muscle fiber types were determined by analyzing SDH activity and myosin-heavy chain (MyHC) isoforms by immunofluorescence techniques in histological slices. The content and activity of muscle proteins involved in protein synthesis/degradation (Akt/FoxO) and energy metabolism (AMPK-p38/PGC1α) were quantified by western blot (WB). All

experimental procedures were approved by the Ethics Committee on the Use of Animals – CEUA-UFMG (220/2019). **Results:** In pre-training period, H impaired performance by reducing (~30%) $S_{MAX}$. After 8weeks, although TRA/H exercised at a lower (26%) absolute intensity than TRA/T, $S_{MAX}$ were similarly increased (~22%) in both TRA groups compared with SED/T. The liver glycogen content also increased by ~34% in the TRA/T, TRA/H and SED/H groups when compared to SED/T. The skeletal muscle SDH activity increased ~9% in both TRA groups when compared with SED/T. SED/H group increased (~15%) cross sectional area (CSA) of oxidative fibers with no additional effects of TRA. The protein content of slow (type 1) and fast (type 2) MyHC by WB did not change in any condition, but % of type 2A fibers was higher (~16%) in both TRA groups than in SED/T group. The protein content of mitochondrial oxidative phosphorylation complexes (OxPhos) as well as mitochondrial membrane (TOM20) and the intracellular regulators of these organelles and oxidative fiber phenotype (i.e., AMPK-p38/PGC1α and TFEB) were not altered in any group. Molecular analysis revealed that TRA/H group reduced the content of FoxO1 (~30%; an inducer of protein degradation and energy metabolism and an inhibitor of angiogenesis). **Conclusion:** Although exercise in H is performed at a lower absolute intensity, training in both environments similarly improved performance and increased the proportion of type 2A fibers, the activity of the mitochondrial enzyme SDH, and the hepatic content of glycogen. Thus, the similar improvement in physical performance of TRA in H and T appears to be due to a change in fiber type to a more oxidative phenotype. Furthermore, training in H could be used as a therapeutic approach to manage patients who were unable to perform moderate-high intensity exercise (i.e., obese and muscle-joint injured recovery) due to mechanical overload.

**Keywords:** Mitochondria, Heat stress, Skeletal muscle metabolism, mitochondria, signaling pathways.

**Supported by FAPEMIG (APQ-01268-2), PRPq/UFMG (27764*27) and CNPq/PROANTAR (442645/2018-0)**