Exercise induces HIF-1α redistribution in the small intestine

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Objective Intestinal epithelial cells are positioned between an anaerobic lumen and a highly metabolic lamina propria, affected by reduced blood flow and tissue hypoxia. Exercise induces blood flow redistribution, leading to hypoperfusion and gastrointestinal (GI) compromise. The hypoxia-inducible factor (HIF) 1α is pivotal in the transcriptional response to oxygen flux. In this study, we hypothesized that exercise induces GI system hypoxia and accumulates HIF-1α.

Methods (1) ROSA26 ODD-Luc/+ mouse model (ODD-Luc) was used to detect HIF-1α expression in the intestine (female, 8-week, n=6/group). ODD-Luc mice were randomized into 4 groups: stayed in 21% O₂ as the normoxic control (C), exercise (E), injected HIF-1α inhibitor PX-478 before swimming (PS), placed in the chamber containing 9% O₂ for 4 hours as the positive control (PC). (2) Exercise models were conducted by volume: Moderate Exercise (ME): mice voluntarily swam for 30 min; Heavy-intensity Exercise (HE): mice swam for 1.5 hours with 5% body weight loads attached to their tails; Long-time Exercise (LE): mice voluntarily swam for 3 hours or till fatigue.

Results (1) Exercise increased HIF-1α in the abdominal area. The luciferase activities boosted after exercise, compared to the controls (ME v.s. C, P<0.05; HE v.s. C, P<0.05; LE v.s. C, P<0.05) but no differences among three exercise groups (ME v.s. HE, P>0.99; ME v.s. LE, P>0.99; HE v.s. LE, P>0.99). (2) Exercise altered HIF-1α distribution in the small intestine in a time-dependent manner. The expression of HIF-1α was significantly increased after exercise and gradually reduced to the rest level. The photons increased at the 0th hour after exercise compared to that of the normoxic control (P<0.01). The level of photons then reduced over time, while the 2nd, 4th and 6th hour post-exercise were still greater than that of the normoxic control (2nd hour v.s. C, P<0.01; 4th hour v.s. C, P<0.01; 6th hour v.s. C, P<0.05), and returned to normal after 24 hours (24th hour v.s. C, P>0.99).

Conclusions Exercise induced the distribution of HIF-1α in the small intestine. The expression of HIF-1α is shown in a time-dependent manner after exercise.