Effects of high-intensity interval exercise, under either induced metabolic acidosis or alkalosis, on the regulation of genes associated with the acid-base regulation in human skeletal muscle

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We have previously reported that rats ingesting sodium bicarbonate ($NaHCO_3$) before training sessions (which reduced the activity-induced decrease in muscle pH) had significantly greater adaptations to exercise training compared to both a control group (no training) and a placebo group (identical training, but ingesting NaCl before each session) (Bishop *et al*., 2010). This included greater increases in MCT4 protein content (Thomas *et al*., 2007). The aim of this study was to investigate the effects of work-matched high-intensity interval exercise, under induced metabolic acidosis or alkalosis, on muscle pH changes, Ser^{300}-PDH protein phosphorylation (which reflects pyruvate dehydrogenase complex deactivation) and the mRNA content of genes associated with acid-base regulation in human skeletal muscle. We hypothesized that a higher level of lactate production could regulate the mRNA content of pyruvate dehydrogenase kinase 4 (PDK4) and the monocarboxylate transporters isoforms 1 and 4 (MCT1 and MCT4), and a lower muscle pH could regulate the mRNA content of sodium hydrogen exchanger 1 (NHE1).

Nine active males (Mean ± SD, age 23 ± 5 y, Body mass 78 ± 15 kg, VO_{2max} 47 ± 7 ml kg^{-1} min^{-1}) performed 9×2-min cycle intervals set at 30% of the difference between the lactate threshold and peak power determined from the lactate threshold test (82±2 % of the peak power), separated by 1 min of passive recovery, on three occasions separated by ~2 weeks. On each occasion, participants ingested ammonium chloride (0.15 g kg^{-1}, ACD) or calcium carbonate (0.15 g kg^{-1}, PLA), which were divided in equal smaller doses and administered 100 and 40 minutes pre-exercise and 10, 70 and 130 minutes post-exercise, or sodium bicarbonate (0.3 g kg^{-1}, ALK), which was administered in a single dose 100 minutes pre-exercise, in a randomised, counterbalanced order, using a crossover design. Venous blood samples were drawn every 20 minutes from 100 minutes pre-exercise, after the 3rd, 6th and 9th interval, and every 30 min post-exercise until 3 h following exercise. Biopsies were taken from the *vastus lateralis* muscle pre, post-exercise and 3 h following exercise.

Blood pH and bicarbonate were significantly lower during ACD *vs* PLA, and higher during ALK *vs* PLA, from 10 minutes pre-exercise until 3 h following exercise. Blood lactate was lower during ACD *vs* PLA after the 3rd exercise interval and significantly higher during ALK *vs* PLA after the 6th and 9thinterval, with no difference between conditions pre and post exercise. Muscle pH was significantly lower post-exercise *vs* pre-exercise and 3 h following exercise across all conditions with a greater decrease during ACD *vs* both PLA and ALK, but with no difference between PLA and ALK. Ser^{300}-PDH protein phosphorylation was significantly lower post exercise *vs* both pre exercise and 3 h following exercise across all conditions, with a greater post-exercise decrease during both ACD and ALK *vs* PLA. The lower values for ACD *vs* PLA pre-exercise approached significance (P=0.07). PDK4 mRNA levels were significantly lower during ACD *vs* PLA pre-exercise, and were increased significantly 3 h following exercise *vs* pre and post exercise across all conditions. MCT4 mRNA levels significantly increased 3 h following exercise *vs* post-exercise with no difference *vs* pre exercise across conditions. No difference was observed for the mRNA levels of MCT1 and NHE1. In contrast to our hypothesis, we did not observe any effect of acid or base ingestion on exercise-induced changes in the mRNA content of genes associated with acid-base regulation in human skeletal muscle. We did however, observe that acid ingestion was associated with a greater exercise-induced decrease in muscle pH, and a greater decrease in Ser^{300}-PDH protein phosphorylation.

Bishop DJ, Thomas C, Moore-Morris T, Tonkonogi M, Sahlin K & Mercier J. (2010). *American Journal of Physiology. Endocrinology and Metabolism* **299,** E225-233.

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