Letter To The Editor

Response to letter to the editor by Gomez-Cabrera et al.

J. O. Holloszy, K. Higashida, S. H. Kim, M. Higuchi, and D.-H. Han

Division of Geriatrics and Nutritional Sciences, Washington University School of Medicine, St. Louis, Missouri

Submitted 23 November 2011; accepted in final form 25 November 2011

TO THE EDITOR: In their Letter to the Editor regarding our paper [Higashida K, Kim SH, Higuchi M, Holloszy JO, Han D-H. Normal adaptations to exercise without supplementation of antioxidant vitamins in rats trained for 3 wk had significantly higher...muscle protein concentrations of these factors...in...rats trained for 6 wk.” This is an amazing claim, because the PGC-1 protein and NRF-1 and mTFA mRNA assays were all measured in the same six muscles taken 48 h after the last exercise. To obtain information regarding the time course of these events it would be necessary to take muscles at different time points after exercise. Furthermore, increases in PGC-1α protein and NRF-1 and mTFA mRNAs are not markers of training but occur acutely in response to single bouts of exercise (8, 9, 13). The only measurement made by Gomez-Cabrera et al. (3) that could have provided information regarding a training-induced increase in mitochondria is cytochrome c. However, although the authors claimed that vitamin C prevented an exercise-induced increase in cytochrome c, the approximately twofold increase in cytochrome c in the vitamin C-treated trained group shown in Fig. 4 of Gomez-Cabrera et al. (3) does not appear to be significantly different from the value for their control trained group. Furthermore, the authors measured “cytochrome c in the cytosolic fraction,” which has no obvious relevance to cytochrome c in the mitochondrial fraction.

In the study by Ristow et al. (10), previously trained and untrained groups of men underwent 4 wk of training with or without supplementation with vitamins C and E. Ristow et al. reported that the training resulted in large increases in insulin-mediated glucose disposal (euglycemic clamp) and in muscle mRNA levels of PGC-1α, PGC-1β, PPARγ, and superoxide dismutase (SOD)1 and -2 and that the antioxidant vitamins prevented these adaptations. The findings reported by Ristow et al. are puzzling, because the euglycemic-hyperinsulinemic clamps and muscle biopsies were done 7 days after training was stopped. The improvement in insulin-stimulated glucose disposal that occurs in response to training reverses rapidly after cessation of training and disappears within 3–4 days and is no longer present after 7 days (1, 5, 7). The finding of a persistent, highly significant increase in “insulin sensitivity” in the no suppl. trained group (but not in the suppl. trained group) reported in their Fig. 1 by Ristow et al. is, therefore, extremely puzzling. In a study done to evaluate the claims by Ristow et al. (10), Bente Pedersen’s group found identical improvements in insulin-stimulated glucose uptake with training in their antioxidant and placebo groups (15). Ristow et al. measured mRNA levels of PGC-1α, PPARγ, and SOD1 and SOD2 in muscle biopsies taken 7 days after the last training sessions. The increases in mRNAs induced by exercise occur in response to single bouts of exercise and occur regardless of whether or not an individual is trained or not and therefore are not markers for the trained state (8, 9, 13). The exercise-induced increases in mRNAs are transient and reverse rapidly. For example, Perry et al. (8) and Pilegaard et al. (9) have shown, in studies on young men, that PGC-1α mRNA was increased 2-h after each of a series of exercise sessions and had returned to baseline (i.e., preexercise) level 24 h after each exercise bout. Therefore, the finding reported by Ristow et al. that PGC-1α, PPARγ, and PGC-1β mRNAs were still increased approxi-
mately threefold in muscle 7 days after the last training session in the no suppl. (but not in the suppl.) group (their Fig. 2) seems difficult to explain or accept. In contrast, in our study on rats, we measured five mitochondrial proteins and PGC-1α, SOD2, and GLUT4 proteins in muscle taken the day after the last bout of exercise and found similar two- to threefold increases in the vitamins C and E-supplemented and control groups (4).

In light of the results of our study (4), the studies of Yfanti and colleagues (14, 15) and earlier studies (6, 11, 12), we conclude that there is no evidence that antioxidant vitamins interfere with the adaptive responses to endurance exercise training.

REFERENCES