Effects of training and exhaustive exercise on the mitochondrial oxidative capacity of brown adipose tissue

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Oxidation of pyruvate, α-ketoglutarate, palmitoylcarnitine, succinate, and ferrocytochrome c by interscapular-brown-adipose-tissue (BAT) mitochondria of untrained and trained rats were measured at rest and after running to exhaustion. At rest, BAT mitochondria from trained rats showed significantly lower activities (< 50%) for the oxidation of all the substrates. In untrained rats the activities of the enzymes for the oxidation of all the substrates except pyruvate and succinate were lower at exhaustion compared to the resting state when expressed on a per-gram-fresh-weight basis. In trained rats all of the enzyme activities increased as a result of exhaustive exercise. These differences between the two groups of rats in the post-exercise changes in oxidative capacities suggest that following an initial adaptation, resulting in a large decrease in mitochondrial oxidative activity, training protects the residual oxidative pathways against exercise-induced inactivation. These data show that unlike exposure to cold, or overfeeding, a physiological stimulus such as exercise reduces the oxidative capacity of BAT, and therefore may reduce the thermogenic activity of the tissue in endurance-trained rats as has been addressed in the scientific literature.

Oxidative capacity and the fresh weight of brown adipose tissue (BAT) of young rats are increased by prolonged cold exposure (1) and by feeding 'cafeteria' diets (2). Rats subjected to these regimes also show an increase in the capacity for non-shivering thermogenesis (NST). Numerous studies have demonstrated that BAT is the major site of NST which has been attributed to the presence of a GDP-binding protein (thermogenin) in the inner membrane of BAT mitochondria (3). In addition to the activation of the oxidative activity of this tissue by direct sympathetic innervation (4), it is also controlled by catabolic hormones, including norepinephrine, epinephrine, thyroxine, and glucagon, of which the circulating levels are all increased during exercise (5).
It has also been amply demonstrated that endurance training increases the oxidative capacity of muscle in rats (6) and humans (7). Studies in rats also demonstrated that physical exercise can increase the oxidative capacity of liver (8). Similar increases in the oxidative capacity of muscle (9) and in other tissues (10) have also been observed in mammals exposed to 4°C for 6 weeks or longer. These studies demonstrated that physical exercise and cold exposure increase the mitochondrial content of several tissues. However, to our knowledge, the effect of training and physical exercise on the oxidative capacity of BAT as measured by its capacity to oxidize pyruvate, α-ketoglutarate, palmitoylcarnitine, succinate, and ferrocytochrome c had not been previously addressed in the scientific literature. It has been observed that exercise training caused a reduced thermogenic response in rats (11,12) as well as a diminished dietary thermogenic response in humans (13). These observations are indicative of a possibly reduced oxidative capacity in BAT. Because of the similarities of the endocrine responses during cold exposure and physical exercise the effect of the latter on an important determinant of the thermogenic activity, namely mitochondrial oxidative activity in BAT, was studied.

Materials and Methods

Animal care, endurance training, and running to exhaustion

Sixteen female Sprague-Dawley rats (Bantin & Kingman, Fremont, CA) weighing 140-150 g were housed in pairs, had access to Purina Rat Chow and water ad libitum, and were habituated to a 0500-1700-h light cycle. Rats were randomly assigned to either a habitually-sedentary or a chronically-exercised group consisting of 8 rats each. The training group was exercised on a Quinton rodent treadmill (model 42-15) 5 days a week for 5-6 weeks. The intensity of the training bouts was progressively increased so that by the beginning of the fifth week of training, rats ran at 30 m/min up a 15° gradient for 2 h (6). To familiarize them with treadmill running, the sedentary group was exercised once a week at 26 m/min, 15° gradient, for 5 min.

Two days following the last training bout, rats were sacrificed either at rest or after exhaustive exercise at 26 m/min, 15° gradient. Exhaustion was identified by the loss of the righting reflex.

The two lobes of interscapular and subscapular BAT were removed from each rat, separated from adhering muscle and white adipose tissue, weighed, and stored in aluminum foil on ice until homogenized (usually within an hour).

Isolation of brown-adipose-tissue mitochondria

Homogenate (5% w/v) of interscapular or subscapular BAT was prepared in a medium containing KCl (100 mM), Tris (50 mM), KH₂PO₄ (50 mM), MgSO₄ (5 mM) and Na₂EDTA (2 mM), pH 7.5. About 100 mg of finely cut BAT was homogenized using a hand-operated Potter-Elvehjem homogenizer with a loosely fitting pestle. An aliquot (100 µl) of the homogenate was transferred to an Eppendorf micro-reaction tube and stored on ice for the assay of cytochrome oxidase activity. The remainder was used for isolation of