Slow Decay of Acetyl-Carnitine in Skeletal Muscle After Exercise

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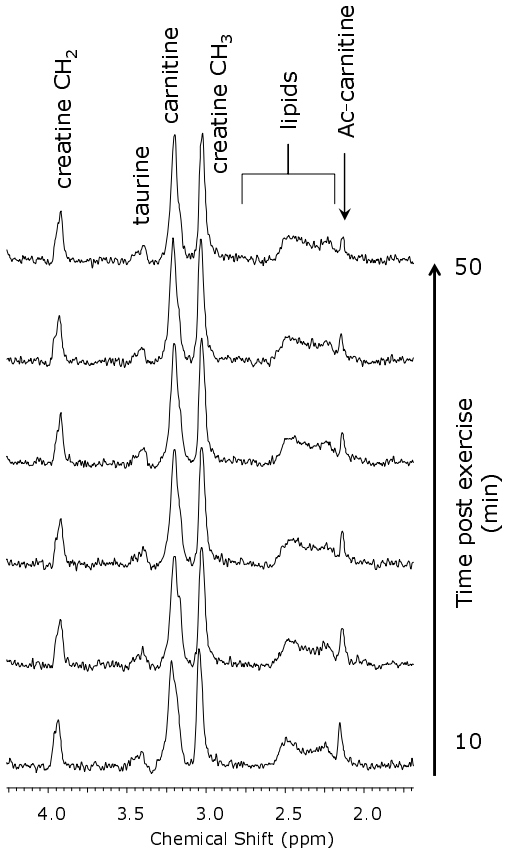
Carnitine serves two critical functions in muscle energy metabolism (1, 2). In addition to its role in transferring long-chain acyl groups into mitochondria, carnitine also is a substrate for the reaction catalyzed by carnitine acetyl transferase: acetyl-CoA + carnitine ↔ acetyl-carnitine + CoA. Rapid interconversion of acetyl-CoA with acetyl-carnitine buffers acetyl-CoA when the rate of generation of acetyl-CoA exceeds the rate of oxidation in the TCA cycle. Since the concentration of CoASH is normally very low, rapid generation of even a small excess of acetyl groups at the onset of exercise would acetylate the entire CoA pool and completely inhibit flux through both pyruvate dehydrogenase and the citric acid cycle at the level of α-ketoglutarate dehydrogenase (2). Intense exercise has been shown to increase acetyl-carnitine measured by ^{1}H NMR spectroscopy (3) or from muscle biopsies (4,5). After intense exercise in humans, acetyl-carnitine recovers to baseline after 3 hours but little is known about the kinetics of recovery presumably because the analysis requires biopsy (4,5).

Methods

Four healthy subjects were studied. Single-voxel STEAM spectra were acquired from soleus muscle using a 7T human scanner (Philips Medical Systems, Cleveland, Ohio) and a half-cylinder transmit/receive coil customized to fit the shape of the human calf. Acquisition conditions were: TR = 2s, TE = 20 to 40 ms, typical voxel size ~2 mL, NSA 128. The resonance at ~2.13 ppm was assigned to the methyl group of acetyl-carnitine (3). Standard calf flexion / extension exercise was performed outside the magnet. Approximately 4 minutes was required for positioning and shimming once the subject was placed in the system. The concentration of the total carnitine + acyl carnitine pool was assumed to be 24 mmole/kg dw (1).

Results

Stacked ^{1}H NMR spectra (each acquired in ~6 min) are shown. The resonance areas of carnitine, creatine and taurine did not change during recovery. A prominent resonance at about 2.14 ppm was detected immediately after exercise and decayed slowly with time as shown in the adjacent Figure. This resonance, assigned to acetyl-carnitine, decayed with a rate constant of 19.3 ± 2.4 min.



Discussion

Based on the reported linear relationship between [acetyl-carnitine]/[carnitine] and [acetyl-CoA]/[CoASH] in human muscle (4), these observations suggest that acetyl-CoA / [CoASH] recovers slowly after exercise. Since the total CoASH pool is constant, acetylation of much of the CoA pool reduces the availability of CoA for long chain fatty acid oxidation. Dysregulation of carnitine metabolism is linked to fatal human diseases, and manipulation of carnitine metabolism has been explored for improving exercise performance as well as treatment of diabetes, obesity and heart failure. The capacity to directly monitor acetyl-carnitine kinetics provides significant new information about skeletal muscle metabolism.

References

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