Non-negative least squares (NNLS) and gated CSI analyses of phosphocreatine recovery kinetics in human skeletal muscle.

S. C. Forbes[1], A. T. Paganini[2], J. M. Slade[2], T. F. Towse[1], and R. A. Meyer[1,2]

[1]Physiology, Michigan State University, East Lansing, Michigan, United States, [2]Radiology, Michigan State University, East Lansing, Michigan, United States

Introduction:

^{31}P-NMR measurements of the time constant or initial rate of phosphocreatine (PCr) recovery in skeletal muscle are often used as indices of muscle oxidative capacity (1). This practice assumes that PCr recovery is entirely dependent on oxidative metabolism (2,3), and that PCr recovery follows a mono-exponential time course. However, under some conditions multi-exponential or higher-order PCr recovery has been observed (4,5). One explanation for multi-exponential PCr recovery is muscle heterogeneity. For example, in rodent hind limb muscles, in which the different fiber types have starkly different mitochondrial contents and oxidative capacities, multi-exponential PCr recovery is observed, with slow and fast components corresponding to fiber populations with low and high mitochondrial contents (6). In contrast, quantitative histochemical studies show that the oxidative capacities of the different fiber types in human skeletal muscles are relatively homogeneous compared to rodent muscles (7). Therefore, it is not clear that muscle heterogeneity can account for multi-exponential or higher-order PCr recovery behavior in human muscle. An alternative explanation for higher-order behavior is that PCr recovery is not entirely dependent on oxidative metabolism, but that anaerobic glycogenolysis contributes to PCr recovery after more intense exercise (5). The purpose of this study was to test this possibility by comparing the kinetics of PCr recovery in human muscle after exercise at low vs. high intensity.

Methods:

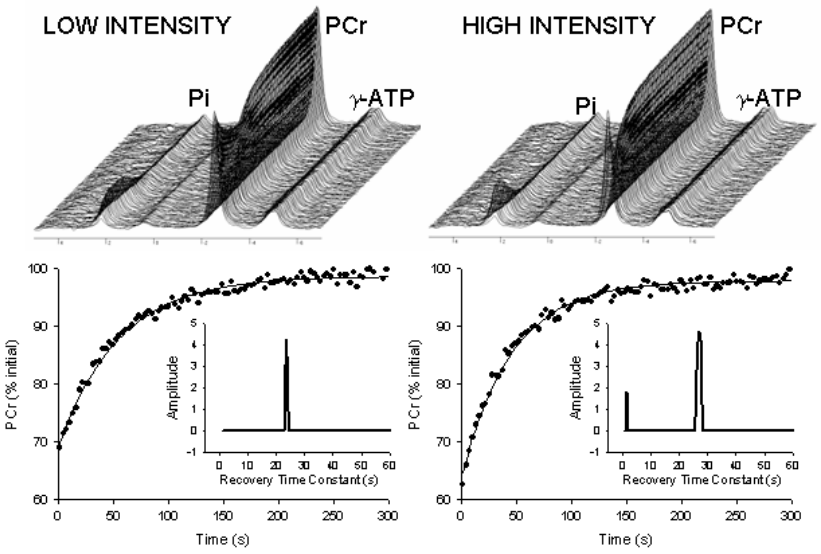
Ten adult subjects (age 28±8 [SD], 1 female) performed five 6.5 min duration cycles of dynamic ankle plantar flexion exercise (peak target force 20% MVC) and recovery at two intensities (low = 1 contraction every 3 s for 90 s, followed by 5 min recovery; high = 3 contractions every 3 s for 30 s followed by 6 min recovery), while one-shot ^{31}P spectra (51.7 MHz, TR 3s) of the triceps surae muscles were continuously acquired via a 10 cm diameter circular surface coil on a GE 3T Excite system (GE Medical, Milwaukee, WI). Subjects were supine and force was continuously recorded on a custom-built non-magnetic ergometer. Spectra from corresponding time points during the 2-5th exercise-recovery cycles were added, yielding 4 NEX gated spectra with 3 s time resolution. Peaks were integrated and pH calculated using the AMARES algorithm (8) of the jMRUI package. The time course of PCr recovery was fit to a sum of exponential components using the non-negative least squares (NNLS) algorithm (400 time constants linearly spaced from 1.5 to 80 s, plus a constant background, which fits the end-exercise PCr level). In a parallel study of 10 subjects (age 22±3, 2 female), PCr recovery time constants were measured in soleus, lateral, and medial gastrocnemius muscles after similar dynamic plantar flexion contractions performed at 20 s intervals using the spatially-resolved, gated CSI method (5).

Results:

Total force-time integral was similar during the low (1936±249 N-s/cycle [SE], n=10) vs. high intensity (1543±85) exercises. As expected, end-exercise PCr (75±4 vs. 59±4 % initial) and pH (7.06±0.01 vs. 7.03±0.01) were greater after the low vs. high intensity exercise. Representative spectra from a subject for the low (left) and high (right) intensity exercises are shown in the Figure (top). The time course of PCr recovery, and the corresponding NNLS time constant spectra (inset plots) for the same subject appear in the bottom Figures. In all subjects, the NNLS spectrum of PCr recovery after the low intensity exercise was characterized by a single component (mean time constant 27.6±2.7s) accounting for over 97% of the recovery amplitude. In contrast, after the high intensity exercise, an additional, very fast recovery component was detected in 6 of the 10 subjects (time constant 1.7± 0.3 s), which accounted for 13±4% of the total recovery amplitude. In the parallel study there was no significant difference in PCr recovery between the 3 triceps surae muscles (time constants 26±3, 23±3, and 25±2 s for soleus, lateral, and medial gastrocnemius, respectively).

Conclusion:

PCr recovery after low intensity exercise is well-characterized by a single exponential, and is the same in the three muscles, indicating that the oxidative capacities of the recruited fibers in the triceps surae are relatively uniform. The fast recovery component observed after high intensity exercise cannot be due to recruitment of more highly oxidative fibers, because according to the size principle, any additional fibers recruited during more intense exercise would have lower oxidative capacity. Therefore, we conclude that anaerobic glycogenolysis drives the initial, fast component of PCr recovery. It follows that PCr recovery is not entirely dependent on oxidative metabolism, and that the initial rate of PCr recovery after intense exercise should not be used as an index of muscle oxidative capacity.



References:

1) Prompers, JJ, et al, NMR Biomed. 19: 927, 2006.
2) Quistorff, B, et al, Biochem. J. 291: 681, 1992
3) Hsu, AC, Dawson, MJ, Magn. Reson. Med. 49: 626, 2003.
4) Iotti, S, et al, Biochim. Biophys. Acta 1608: 131, 2004.
5) Slade, JM, et al, NMR Biomed. 19: 573, 2006.
6) Meyer, RA, et al, Proc. ISMRM 5: 1309, 1997.
7) Gregory, GM, et al., Muscle Nerve 24: 387, 2001.
8) Vanhamme, L, et al, J. Magn. Reson.129: 35, 1997.