# SIMULTANEOUS MEASUREMENT OF PH, LACTATE AND ACETYL-CARNITINE IN SKELETAL MUSCLE AT 7T

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Acidification and accumulation of lactate and acetyl groups are common metabolic changes occurring in skeletal muscle after high-intensity exercise, affecting muscle performance and subsequent recovery. For a long time, these metabolic changes have been measured either invasively by biopsies or noninvasively by separate MRS techniques targeting on each individual metabolites. For example, muscle pH is almost exclusively measured by $^{31}$P NMR spectroscopy while tissue lactate is usually detected using a $^{1}$H spectral editing technique. It would be an advantage to be able to monitor metabolite levels and tissue pH with high temporal resolution by $^{1}$H NMR alone. This would help answer certain controversial issues in exercise metabolism such as the relation between muscle acidification and lactate accumulation. **PURPOSE**: The current study was designed to monitor recovery of pH, lactate and acetyl-carnitine in forearm muscle after a short period of intense exercise using a single $^{1}$H MRS protocol.

**METHODS:** Single-voxel $^{1}$H MR spectra were acquired at 7T from forearm flexor digitorum profundus muscle (FDP) of healthy subjects (n = 4) at rest and continuously for 12 mins after high-intensity hand-grip exercise (by intermittently squeezing a rubber ball every 2 sec for 2 min). A partial volume $^{1}$H coil ($\phi$ = 9 cm) and a STEAM sequence were used. Other MRS parameters were TR = 2 s, TE = 100 ms, NSA = 32, voxel size ~ 8 - 15 ml. The creatine methyl signal at 3.0 ppm was used as internal standard (30 mmol/kg ww). The protocol was approved by our local IRB. **RESULTS**: As show in Fig 1a, lactate and acetyl signals were virtually absent in the $^{1}$H spectra at rest but appeared after exercise at 4.1 ppm (lactate methine resonance) and 2.12 ppm (acetyl resonance of acetyl-carnitine). The exercise also led to a 0.4 ppm change in chemical shift of the carnosine imidazole $H_4$ signal (Fig 1a left panel), consistent with a drop in pH of 0.82 units (Fig 1b). While both lactate and pH recovered back to near baseline levels in 12 min after rest, the acetyl-carnitine signal continued to increase for ~ 4 min, followed by a slow recovery (Fig 1c). These spectral features were consistently observed for all subjects (n = 4). **DISCUSSION:** As an endogenous molecule not degradable during exercise, carnosine appears to be dependable pH reporter in skeletal muscle. In contrast, exercise-induced pH change could be overestimated by $^{31}$P NMR in skeletal muscle due to the intrinsic heterogeneity in fiber composition, and therefore in its response to phosphocreatine degradation and inorganic phosphate accumulation. Detection of pH-sensitive signal, the carnosine imidazole $H_4$, can be conveniently integrated with detection of lactate methine signal and acetyl-carnitine acetyl signal by a single localized $^{1}$H MRS protocol. Evidence from 7T $^{1}$H MRS observation suggests that lactate production is accompanied by muscle acidification during exercise and that their recovery after exercise is largely synchronous. **CONCLUSIONS:** Noninvasive and simultaneous measurement of pH, lactate and acetyl-carnitine provides easy access to important metabolic information on multiple pathways in skeletal muscle in vivo. These data support the view that the processes of $H^+$ production and handling are closed related to those of lactate in exercised muscle tissues.

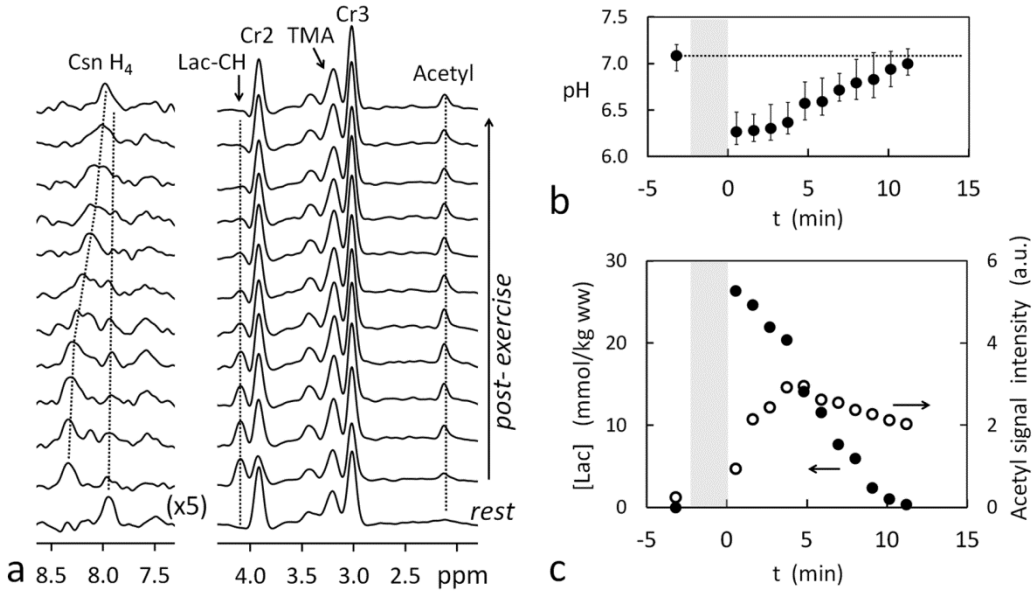


Fig 1. (a) $^{1}$H MR spectra of forearm FDP muscle from a 24 yr female at rest and after 2.5 min of handgrip exercise with temporal resolution of 1.1 min. (b) Dependence of pH on *t*, the time-after-exercise, with pH evaluated from chemical shift of the carnosine H4 proton. (c) Dependence of lactate (solid circle) and acetyl-carnitine (open circle) on *t*. The gray zones in (b) and (c) indicate the period of handgrip exercise. Abbreviations: Lac-CH: Lactate methine group; Csn: Carnosine; Cr2 and Cr3: methylene and methyl groups of total creatine; Acetyl: acetyl-carnitine; TMA: Trimethylamine group of total carnitine.