Multimodal determination of load changes in the muscle - A combination of ^{1}H-MEGA-PRESS and blood sampling

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Target audience: Physiological Researchers and Members of the Magnetic Resonance Spectroscopy Community.

Purpose: In exercise physiology, lactate represents an important marker to characterize an anaerobic exercise of loaded muscles and is widely used to monitor and adjust training conditions [1]. Presently, lactate is discussed to be more than only a product of the anaerobic glycolysis - it is also considered to play a crucial role regarding energy supply and to act as a signal molecule within muscles [2]. In sport sciences, load induced lactate dynamics is typically monitored by collecting blood samples successively from the earlobe. However, this dynamics is highly affected by inter-individually varying biological and metabolic factors, which lead to typical peak lactate delays of approximately 3 minutes after the load end as well as to substantial dilutions [3]. Therefore, direct lactate measurements in the loaded muscles should be advantageous to better characterize muscle specific anaerobic strains. In this context, ^{1}H-MR spectroscopy, allowing non-invasive quantitation of metabolites in the tissue, may provide an important local tool for lactate quantitation in loaded human muscles. Since the lactate resonances are completely overlapped by strong lipid signals at 1.3 ppm, their quantitation requires sophisticated spectroscopic techniques, like spectral editing with MEGA-PRESS sequences, which encompass selective modulation of lactate to eliminate disturbing resonances by subtracting edited from non-edited spectra. In this study, we adapted MEGA-PRESS to characterize the lactate dynamics in human calf muscles after an anaerobic load and to compare them with lactate depletions obtained by blood sampling.

Methods: We investigated 10 healthy, male volunteers (27 ± 4 years) on a clinical whole body 3 T MR scanner (Magnetom TIM Trio, Siemens, Germany) with a flexible surface coil (RAPID Biomedical, Germany). Subjects were lying in supine position and performed series of standardized plantar flexions of the right calf muscle with a dedicated pedal ergometer (100 bpm cadence, 0.6 bar counterforce). Each examination started with a 15 min rest period used to select the MRS voxel position in the *M. triceps surae* of the right calf muscle (see Fig. 1a), to shim the B_0 field homogeneity, and to acquire a reference spectrum (TR/TE: 2000/140 ms, NEX: 16, frequency selective 40 Hz Gaussian pulse at 4.1 ppm to edit the ^{2}CH lactate group). Following 3 min of exercise, series of seven spectra were acquired with a time resolution of 3.5 min. Intensities of lactate doublet at 1.3 ppm (Fig. 1a) were quantified in MEGA-PRESS difference spectra by using the jMRUI package and normalised with the creatine intensity of the reference spectrum (Lac/Cr ratios). In addition to the MRS measurements, blood samples were collected from the earlobe once during rest, every minute during load and six times during recovery (1, 3, 5, 10, 15 and 20 min post load). Blood lactate was quantified with a portable Lactate SCOUT unit (EKF Diagnostics GmbH, Cardiff, UK).

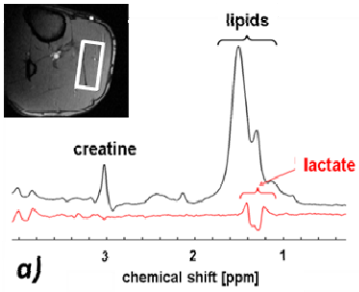
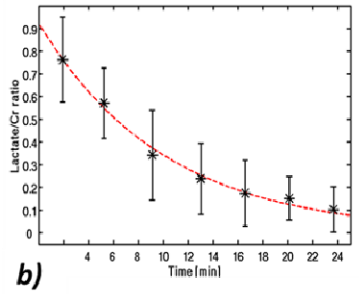


Table 1: Global and local lactate values (mean ± standard deviation)

Blood lac rest	1.48 ± 0.33 mmol/l
Blood lac max	3.73 ± 1.26 mmol/l
Blood lac $t_{1/2}$	38.47 ± 23.6 min
^{1}H lac (2 min postload)	0.76 ± 0.19
muscle lac $t_{1/2}$	10,2 ± 4,9 min



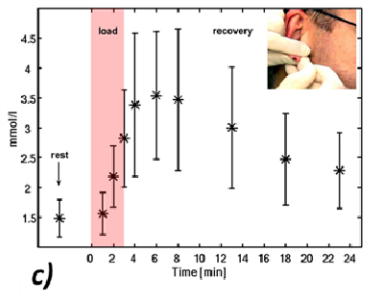


Fig.1 ***a)*** MRS voxel with non-edited spectra (black) and difference (red) MEGA-PRESS muscle spectrum showing large lipid signal and lactate doublet at 1.3 ppm. ***b)*** Mean post load Lac/Cr dynmamic (black) with corresponding monoexponential fit (red). ***c)*** Mean dynamic of lactate concentrations (mmol/l) in blood before, during and after the load.

Results: Figures 1b and 1c show the time course of mean Lac/Cr ratios in the muscle and mean blood lactate concentrations, respectively. Table 1 lists mean values and decay time constants, which were determined by monoexponential fitting post-load. Prior to the exercise, the low rest concentrations prevented the direct spectroscopic lactate detection. 2 min after the load, Lac/Cr ratios amounted to 0.76 ± 0.19, averaged over all subjects and decayed exponentially during the recovery (see Fig. 1b). Blood lactate concentrations revealed the expected increase after exercise with a maximum occurring at 6 minutes post load, followed by a significantly slower decrease than the local Lac/Cr ratios (Tab. 1, Fig. 1c). Post-load blood lactate depletions revealed substantially higher inter-individual variation of the time constants than the Lac/Cr ratios in muscle.

Discussion and Conclusion: We describe our first efforts to determine post-load lactate globally from blood samples as well as locally from strained muscle by combining ^{1}H-MEGA-PRESS MRS with conventional blood sampling. The increase of the measured global values indicates a high amount of anaerobic energy supply, whereas the inter-individual variations of the post load time courses may be ascribed to different training status of the study sample. Differences between the local and global lactate dynamics are indicative of the associated metabolic effects, which take place in tissue, resting muscles, liver and heart and affect the interpretation of exercise induced lactate changes. However, in order to provide a more accurate quantitation of anaerobic processes in muscle, we also have to consider other energy supply pathways, for example by investigating ^{31}P-MRS based quantitation of phosphorous compound changes.

References: 1. Juel C et al. Am J Physiol Endocrinol Metab 2003; 286(2):E245-51. 2. Hashimoto T. Med Sci Sports Exerc 2008; 40:486-494. 3. J. Ren Magn Reson Med 2013; 70:610-619.