Skeletal muscle metabolism measured at rest and after excercise in obese non-diabetic subjects

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Introduction:

Measurement of phosphocreatine (PCr), ATP, and inorganic phosphate (Pi) by ^{31}P-MRS during exercise-recovery experiments provide information about mitochondrial capacity while it is possible to measure the mitochondrial activity at rest by using the ^{31}P-MRS magnetization transfer (MT) technique. It has been discussed, whether the parameters measured by these two methods correlate [1, 2]. Alteration in skeletal muscle substrate oxidation and energy metabolism have been linked to obesity and type 2 diabetes individuals [3], but no comparison between the ^{31}P-MRS-derived physiological parameters have been performed in this population to date. Therefore, the goal of this study was to compare the ATP metabolism rates at rest and post-exercise in obese non-diabetic adults.

Materials and Methods:

Eight healthy non-trained overweight to obese subjects (2m/6f; a= 36±6 y.; BMI= 31±3 kg/m^2; VO_2max= 34±3 ml/min/kg LBM) were recruited for this study and underwent the ^{31}P MRS protocol two hours after standardized breakfast. It has been shown, that the order of MT and dynamic exercise do not influence the measured metabolic fluxes [1], so consecutive measurements of pseudo-random order were performed on two MR scanners, at 3T, for 2 min rest- 6 min exercise- 6 min recovery protocol, and at 7T, for MT experiments [4], both (Siemens Healthcare, Erlangen, Germany). For the exercise measurements, subjects were lying in prone position with the left quadriceps muscle placed over the double-tuned surface coil (10 cm, ^{31}P/^{1}H, Rapid Biomedical, Wimpar, Germany). Non-localized ^{31}P-MRS (TR= 2s, flip angle 42°) was performed throughout the exercise protocol. Knee extensions were performed on an ergometer (Ergospect, Innsbruck, Austria) once every TR (2s) at work load set to achieve approx. 30% depletion of PCr without altering end-exercise pH. The recovery constant τ_{PCr}, initial recovery rate V_{PCr} and maximal oxidative flux Q_{max} were calculated. For the MT experiments, subjects were lying in supine position with a surface coil (identical dimensions) fixed over their left quadriceps muscle. Non-localized ^{31}P-MRS was performed w/o saturation of γATP resonance. Furthermore, apparent ^{31}P MR T_1 relaxation times were measured in the presence of γATP saturation. Forward rate constants k_{ATP} (ATP<>Pi reaction) and k_{CK} (ATP<>PCr reaction) and corresponding fluxes F_{ATP} and F_{CK} were calculated and the MT parameters were compared to Q_{max} by linear regression.

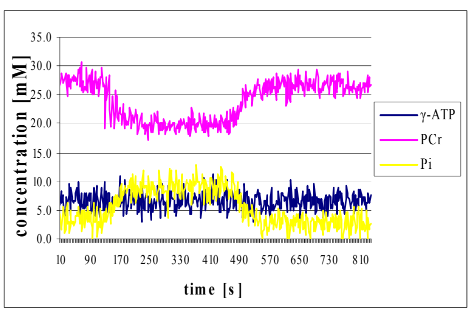


Fig. 1 Time course of ^{31}P-MRS signals acquired in a single volunteer during the exercise-recovery protocol.

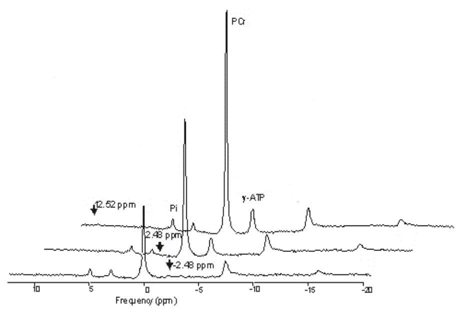


Fig. 2 Representative spectra of MT experiment, with saturation frequency set at three different frequences; -2.48 ppm (bottom), 2.48 ppm (middle) and 12.52 ppm (top).

END EXERCISE			
pH	7.04	±	0.04
PCr consumption [%]	30.97%	±	9.83%
RCOVERY			
V_{PCr} [mM/s]	0.27	±	0.08
PCr recovery constant (t) [s]	36.91	±	7.52
$Q_{max,ADP}$ [mM/s]	0.48	±	0.10
MT			
k_{ATP} [s^{-1}]	0.07	±	0.03
F_{ATP} [mM/s]	0.23	±	0.09
k_{CK} [s^{-1}]	0.27	±	0.05
F_{CK} [mM/s]	10.16	±	2.99

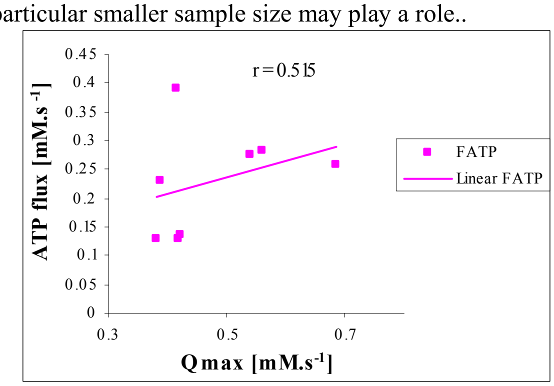
Tab. 1 Calculated parameters given as mean ± stdev

Results and Discussion:

Representative time course of ^{31}P-MRS signals from exercise experiment is depicted in Fig. 1 and spectra from a MT experiment are shown in Fig. 2. The ATP production and PCr recovery parameters calculated form both experiments are summarized in Tab. 1. The metabolic exchange rates calculated from the MT datasets measured in muscle at 7T at rest are comparable with previously published data [1]. We could detect only a trend but no significant correlation (p=0.19) between Q_{max} and ATP flux (Fig.3), When comparing with previous publication [1], differences in study population, muscle group, exercise protocol and in particular smaller sample size may play a role..

Conclusion:

Energy metabolism study by ^{31}P-MRS methods was performed on overweight to obese non-diabetic subjects. At this stage our data show a trend but no significant correlation between ATP flux in resting state and maximal oxidative flux. For final conclusion on correlation of ^{31}P-MRS derived metabolic parameters in rest and after exercise challenge more volunteers need to be measured or specific points of the experiments have to be accounted for.



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