The effects of deoxyhemoglobin and flow rate on R2' in hindlimb perfused skeletal muscle

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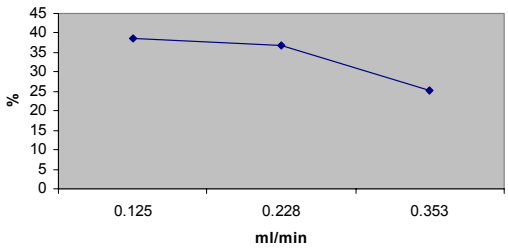
Introduction: During exercise skeletal muscle NMR relaxation parameters are altered by changes affecting the BOLD response, the osmotic movement of water into muscle cells, and a decrease in cellular pH (1). In addition to the metabolic effects of contraction on relaxation parameters, blood flow linearly increases with exercise intensity, thus affecting the apparent T1. Therefore, the variations in signal intensity during a muscle contraction are influenced by several factors, which are difficult to differentiate from each other.

Purpose: To study the effects of different blood flow rates on NMR relaxation parameters on skeletal muscles under resting conditions.

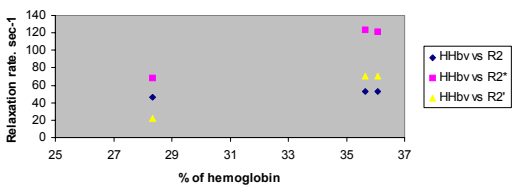
Methods: The abdominal aorta and the inferior vena cava were catheterized below the level of the renal arteries on 3 male mice. The arteries and veins irrigating the organs in the pelvic cavity and the left hindlimb were ligated. A peristaltic pump was used to perfuse the right hindlimb of each mouse with a perfusate containing Krebs-Henseleit buffer, albumin, bovine erythrocytes and insulin (3 mU/Kg/min) at an initial flow rate of 0.125 ml/min. The perfusate was maintained at a pH of 7.21 ± 0.3, PO2 of 94 mm/Hg and 37 °C. The perfusate had average hemoglobin and hematocrit of 11 gr/dl and 35%, respectively. At the beginning and the end of the experiment a high resolution anatomical image was acquired using spin echo sequence TR 500, TE 13 ms, FOV 35x35 cm, matrix size of 256x256 and 6 averages. Other MRI measurements included perfusion R1 (using inversion-recovery EPI) (TR/TI/TE = 8000/100,200, 400, 400….6400ms/17.66ms) R2 multi spin multi echo sequence (TR/TE 2500ms/62,82,102…202ms) R2* multi echo gradient echo (TR/TE 2500/12,24,36….96), and R2' (=R2* – R2). Before and after MRI measurements, arterial and venous blood samples were obtained and used to measure pO2, pCO2, pH, hemoglobin, hematocrit, oxygen saturation, [glucose], [lactate], electrolytes (Na+, K+, and Cl–). All measurements were repeated at additional flow rates of 0.228 and 0.353 ml/min. Signal intensities of the VASO images at different flow rates were used to determine variations in blood volume (2).

Fig. 1. SatO2 as a function of flow rate



Statistical analysis: Mean and standard deviations were calculated for relaxation parameters and other physiological variables for each flow rate. One way ANOVA with Bonferroni post hoc test was performed to compare means of relaxation parameters and physiological variables at different flow rates. Significance was set at a $p<0.05$. Pearson correlations were performed to determine associations between different parameters.

Fig. 2. Relaxation parameters as a function of venous oxygen saturation



Results: Muscle viability was confirmed by significant difference between arterial and venous pO2 and glucose ($p<0.01$) and a lack of change in potassium concentration and pH. There was a concentration inverse correlation between pO2 (a-v) and flow rate (fig.1). There was no significant correlation flow rate. However, R2' was positively correlated to venous deoxyhemoglobin (r linear inversely correlated to venous oxyhemoglobin (r -0.99, p = 0.04) (fig. 2). Relative of R1, R2 or R2* to not significantly different between the different flow rates. 0.998, p = 0.02) and blood volume was

Discussion: This stable surgical preparation allows us to independently modify variables affecting the BOLD response. It is clear from this study, that the most important physiological variable affecting R2' is oxygen saturation of the venous blood.

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