Study of the contribution of oxygenation to the BOLD contrast in a moderate exercise protocol of the mouse gastrocnemius muscle

B. Jordan[1], B. Gallez[1]

[1]Biomedical Magnetic Resonance Unit, Catholic University of Louvain, Brussels, Belgium

Introduction:

The potential physiological and therapeutic applications of fMRI in skeletal muscle will depend on the identification of the factors that may contribute to the BOLD signal fluctuations. Up to now, the interpretation of signal changes in fMRI studies of muscle have mostly relied on the increase in muscle T_2 associated with osmotically driven fluid shifts (1;2). However, recent studies documented increases in BOLD signal intensity after single contractions coinciding with increases in muscle hemoglobin saturation (3-5). Our study further addresses the issue of the contributing factors to the variations in the BOLD signal intensity in exercising muscle.

Materials and Methods:

BOLD imaging (4.7 Tesla, Bruker Biospec, GRE sequence) was performed during and after application of a moderate electrical stimulation protocol (5 Hz, 0.2ms pulses, 0.5V, for 15 minutes) of the sciatic nerve on mice. In addition, oxygen pressure (measured by EPR oximetry with a 1.2 GHz spectrometer, Magnettch, Germany), blood flow (monitored with Laser Doppler probes), and T_2 (multi echo T_2 images, fast and slow components, T_2 and T_2') of skeletal muscle were monitored. A comparison between mice lacking eNOS ($eNOS^{-/-}$ mice) and their wild type (WT) littermates was performed.

Results:

In WT mice, this moderate exercise protocol significantly increased the BOLD signal intensity (+6.4±0.7 %), as well as muscle oxygenation (+41.8±3.9 %) and T_2' (from ~90 ms to 120 ms) for a prolonged time. Blood flow increased at onset of exercise (~2 fold increase) and immediately dropped after resumption of electrical stimulation. In $eNOS^{-/-}$ mice, BOLD signal intensity also increased during stimulation (+3.3±0.4 %) but the persistence of a high signal intensity after the exercise protocol was not observed. This correlates well with the evolution of muscle pO_2 that progressively decreases after stimulation in $eNOS^{-/-}$ mice. However, T_2' remained high for a prolonged time after stimulation. All results are summarized in Fig.1 and Table 1.

Discussion

This study documents that increases in the BOLD signal intensity can be observed in mouse skeletal muscle performing a moderate and prolonged (15 minutes) exercise protocol. We demonstrated that the BOLD response is likely to depend on oxygenation and blood flow effects at the onset of exercise, and on the single effect of oxygenation after resumption of electrical stimulation. Blood flow and T_2 changes are indeed not correlated with the maintain in the BOLD signal intensity after exercise, on the contrary to muscle pO_2. These data open new possibilities for understanding physiological and pathological phenomenon in skeletal muscle using fMRI.

Fig.1 Effect of a moderate exercise protocol on muscle BOLD signal intensity (A), pO2 (B), blood flow (C), and T_2' (D), measured before, during, and after (post I:0-15min, post II:15-30 min) electrical stimulation.

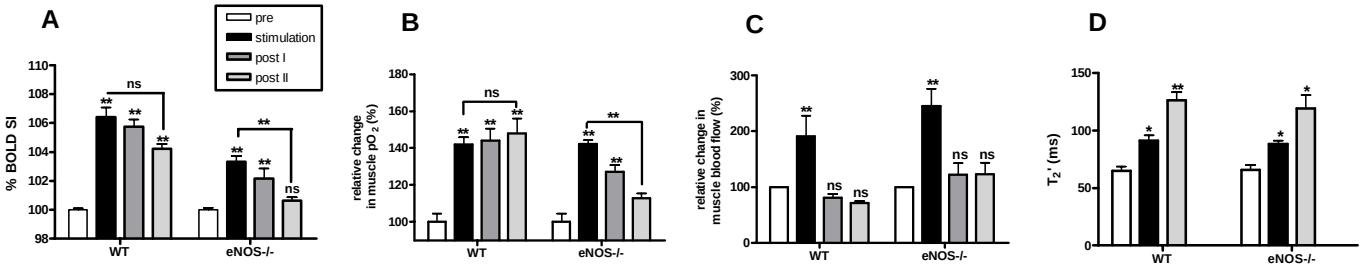

Table 1. T_2 relaxation times of the fast (T_2) and slow (T_2') (mean±sem) component measured in mouse skeletal muscle.

relaxation time	littermate	*Pre (ms)*	*Stimulation (ms)*	*Post (ms)*
T_2	WT	18.5±0.6	20.1±0.3	21.3±0.5
	$eNOS^{-/-}$	19.9±0.9	19.0±2.0	18.8±0.4
T_2'	WT	65.0±3.9	91.4±4.7*	126.3±7.0**
	$eNOS^{-/-}$	65.7±4.2	88.4±3.0*	119.3±11.6*

Références:

(1) Prior BM, Ploutz-Snyder LL, Cooper TG, Meyer RA. J Appl Physiol 2001;90(2):615-23.
(2) Gambarota G, Cairns BE, Berde CB, Mulkern RV. Magn Reson Med 2001;46(3):592-9.
(3) Hennig J, Scheffler K, Schreiber A. Proceedings of the 4th annual Meeting of ISMRM, Denver, 2000, p.122.
(4) Meyer R, McCully K, Reid R, Prior B. Proceedings of the 5th annual Meeting of ISMRM, Glasgow, 2001, p.135.
(5) Towse TF, Wiseman RW, Meyer RA. Proceedings of the 7th annual Meeting of ISMRM, Toronto, 2003; p.1521.