Modeling the hyperemic response in skeletal muscle fMRI

K. Schewzow[1,2], M. Andreas[2,3], E. Moser[1,4], M. Wolzt[2], and A. I. Schmid[1,4]
[1]MR Center of Excellence, Medical University of Vienna, Wien, Austria, [2]Dpt. of Clinical Pharmacology, Medical University of Vienna, Wien, Austria, [3]Dpt. of Surgery, Medical University of Vienna, Wien, Austria, [4]Centre of Medical Physics and Biomedical Engineering, Medical University of Vienna, Wien, Austria

Introduction

Ischemia results in damage to or dysfunction of tissue because of a lack of oxygen and nutrients. Residual impairment of blood flow may limit (functional) recovery. The investigation of ischemia and reperfusion is still hampered by the lack of experimental human models. Recently, BOLD MRI of the skeletal muscle has been introduced to ischemia and post-occlusive reactive hyperemia [1]. Due to the long duration of the experiments, large size of the data and the sensitivity of EPI to artifacts it is desirable to have a stable and operator-independent evaluation method for muscle fMRI data. In this work, we modeled the hyperemic response in skeletal muscle after occlusive ischemia for the more reliable estimation of the important parameters e.g. time to peak, peak value, peak area.

Methods

Ten healthy male subjects were included in this study. The study was performed of 2 different days:

Day 1: resting measurement → ischemia and exercise → reperfusion

Day 2: resting measurement → ischemia and exercise → stenosis → reperfusion

A resting measurement was performed for 2 min; unilateral calf ischemia was induced for 20 min. Voluntary plantar flexions were performed during the last two minutes of ischemia. For complete reperfusion the cuff was deflated and MRI measurements were continued for 30 min. For post-ischemic stenosis, the cuff was partially deflated during the first 5 minutes of reperfusion. BOLD MRI measurements were performed at 3 Tesla using a Tim Trio-scanner (Siemens Medical Solutions, Erlangen, Germany). Echo planar images were acquired every 0.5 s for the duration of the experiment. Five axial slices were selected across the calf with 1.4 mm in plane resolution and slice thickness of 5 mm. Manually drawn regions of interest, covering the soleus, gastrocnemius and tibialis anterior, were extracted. All images were coregistered for motion correction. Afterwards the signal was summed to achieve a time course for each individual muscle. To describe the BOLD signal in calf muscle during reperfusion the intensity curves were fitted in Matlab (Mathworks, Natick, MA, USA). Although the muscle BOLD effect is not yet fully understood it is believed that it reflects - at least partially - the perfusion state of the muscle tissue. Also, the curve shape of the hyperemic response is similar to those in the dynamic contrast enhanced MRI. Therefore, a similar fit function was used as in DCE-MRI (Fig.1).

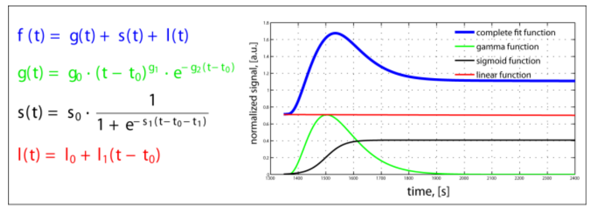

Figure 1. Fit function

Results

Using function *f(t)* 89% of data sets could be fitted successfully. Unfortunately, due to poor quality in some data sets, the fit did not converge. Figure 2 shows a typical fit result of a hyperemia curve. Several parameters which describe the time course of hyperemia were determined from the fit curve. To investigate the influence of post-ischemic stenosis the parameters were averaged over all muscles and compared between day 1 and day 2. The results are shown in table 1. Also differences between the muscle groups were investigated, for this purpose the parameters of day 1 and day 2 were averaged (Table 2).

parameter	Day 1	Day 2
peak width, [s]*	445±78	817±66
start of recovery, [a.u.]*	0.87±0.03	0.68±0.02
peak area, [a.u.]*	77.7±19.7	168.7±15.3

*Table 1: Influence of stenosis. Data are mean±SD. *p<0.05*

parameter	tibialis anterior	soleus	gastrocnemius
peak area, [a.u.]	110±19	81±18	160±19♦
time to peak, [s]	140±10.8	110±11	187±11.2▲
peak width, [s]	458±74	373±71	903±77▲
slope after peak, [a.u./s]	-166±23*	-260±22*	-87±23*

*Table 2: Differences between muscles. Data are mean±SD ♦p<0.05 versus soleus; ▲p<0.05 versus soleus and tibialis anterior; *p<0.05 in each muscles*

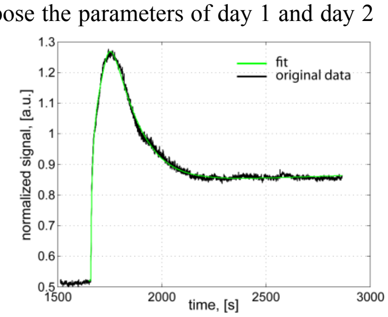

Figure 2. Fit example

Discussion

The aim of this work was to apply a suitable model for the hyperemic response in skeletal muscle BOLD-MRI and to fit the data to this function. The modeling of reperfusion patterns in muscle fMRI enables the comparison between the different muscle groups and also shows the impact of post-ischemic stenosis on certain curve parameters. These results are consistent our the previous work [2,3]. Functional MRI is a promising tool for non-invasive study of ischemia and reperfusion mechanisms in skeletal muscle. This work contributes to the quantitative analysis of the hyperemia data and may be important for the future development of therapeutic strategies in humans.

[1] K. M. Donahue et al. Simultaneous gradient-echo/spin-echo epi of graded ischemia in human skeletal muscle. J Magn Reson Imaging, 8(5):1106-1113, 1998.

[2] A. I. Schmid et al. Post-ischemic stenosis studied by dynamic 31-P spectroscopy and functional imaging. In: Proceedings of the Joint Annual Meeting of ISMRM-ESMRMB, Stockholm, Sweden, 2010 (Abstract #2334).

[3] A. I. Schmid et al. BOLD response of different muscle types to ischemic exercise. In: Proceedings of the Annual Meeting of ISMRM, Hawaii, 2009 (Abstract #3851).

Acknowledgments: this project was supported by the WWTF to M.W.