Changes in Arterial Oxygen Tension with Evoked Stimulation in the Rat Somato-sensory Cortex: Implications for Quantitative fMRI

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Introduction

It is accepted that the BOLD fMRI signal results from changes in the amount and saturation of hemoglobin in a voxel that stem from neurophysiological changes in CBF, CBV and CMR_{O2} with brain activation. This sensitivity of BOLD fMRI to CMR_{O2} has been used to quantify the changes in CMR_{O2} with brain activation (1,2,3). In general, this physiological parameter has been of interest because it is inherent from tissue and, therefore, closer to the activation site, but its quantification relies mostly on the calculation of the venous oxygen saturation under the assumption of a constant and highly saturated arterial oxygenation (~100%). In this work, our goal was to investigate the changes in arterial, tissue and venous oxygen tension and saturation with evoked somato-sensory stimulation in the anesthetized rat using oxygen microelectrodes and deoxy-hemoglobin sensitive optical imaging as a BOLD fMRI surrogate. This data was then used to investigate the impact of these measurements on the quantification of CMR_{O2} from blood oxygenation data (i.e. BOLD fMRI).

Methods

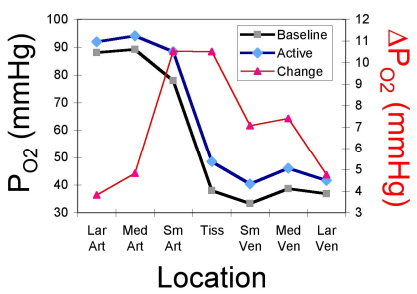
A total of nine male Sprague-Dawley rats (330 to 480 g) were used in this work following an experimental protocol approved by the University of Pittsburgh Institutional Animal Care and Use Committee. The animals were anesthetized using isoflurane (2% for surgery and 1.4% during experiments) and placed in a stereotaxic frame. The skull was removed over the somato-sensory area and covered with agarose gel. Two needle electrodes were placed in the right forepaw of the animals for electrical stimulation and a preliminary optical imaging experiment (620nm light) was performed to determine the activation area. The changes in P_{O2} were measured using three Clark-type oxygen microelectrodes which were positioned over a pial artery, pial vein and tissue (300µm deep). The arterial and venous oxygen probes were re-positioned to sample larger parent pial arteries and veins, respectively. The changes in CBF were monitored using a laser Doppler flowmeter probe (LDF).

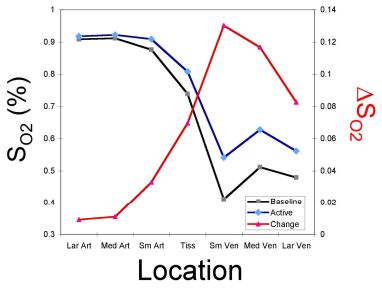
Results

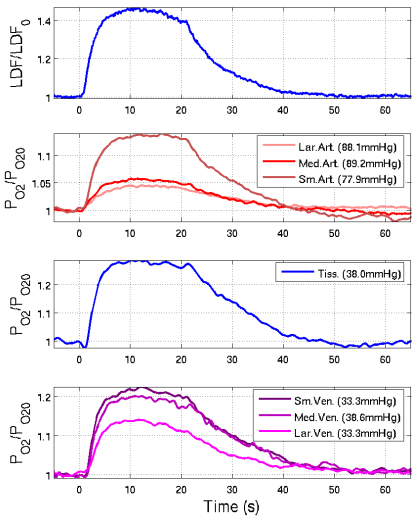
The temporal evolution of the oxygen tension at the targeted large pial artery (D=128µm), medium pial artery (D=96µm), small pre-penetrating artery (D=56µm), tissue, small emerging vein (D=66µm), medium pial vein (D=139µm) and large pial vein (D=391µm) were averaged (see Figures). The average systemic (femoral) arterial oxygen tension was measured to be 134mmHg. Somato-sensory stimulation for 20 s (60 pulses, 1ms in duration, 1.6mA in amplitude, and frequency of 3Hz) produced increases in oxygen tension throughout the sampled vascular tree and was observed to be largest at the pre-penetrating arterial location (left and right figures). The average CBF change was measured to be 41.7%. The change in the average oxygen saturation was calculated and the largest increase in oxygen saturation was observed at the emerging vein location (middle figure). Optical imaging verified that the observed changes in vessel oxygenation were consistent across the pial vasculature over the somato-sensory cortex (not shown). Temporally, the CBF response was faster to peak during stimulation and faster to return to baseline after stimulation compared to the oxygen tension responses in vessels and tissue. The time-to-50% peak of the oxygen tension for the targeted vessel locations relative to that of the CBF response varied as follows during stimulation onset: 0.7s, 0.7s, 0.6s, 0.7s, 0.7s and 1.0s, respectively. Collectively, these results indicate that there is a measurable increase in arterial oxygen tension with evoked neural stimulation, especially in small pial arteries where the increase in oxygen saturation reached a few percent and also slightly lead all of the other measured changes in vascular oxygenation.

Discussion and Conclusion

These data indicate that there is a steep oxygen tension and saturation gradient from arteries to veins that is manipulated with brain activation. Although the arterial oxygen saturation is relatively high, significant increases in the arterial oxygen tension and saturation were observed in small pial arteries. These increases in arterial oxygenation impact the calculation of CMR_{O2} from blood oxygenation data, particularly at high resolution, since the vascular supply will generally shift towards smaller arteries and veins with increasing spatial resolution. Quantification of the relative change in CMR_{O2} from high-resolution BOLD fMRI data (i.e. hundreds of microns) will be underestimated when a constant and fully saturated arterial blood input is assumed.







Figures: (**Left**) Average arterio-venous oxygen tension (P_{O2}) gradient from pial vessels over the somato-sensory cortex during resting and activation conditions. (**Middle**) Calculated arterio-venous oxygen saturation (S_{O2}) gradient using the P_{O2} data in Left. (**Right**) Average temporal changes in blood flow (top) and vascular (arterial in 2nd panel from top and veins in bottom-most panel) and tissue oxygen tension (3rd panel from top) with somato-sensory stimulation.

References: (1) Davis TL, et al., PNAS 95:1834 (1998); (2) Kim SG, et al., MRM 41:1152 (1999); (3) Valabregue R, et al., JCBFM 23:536 (2003).
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