Arterial contribution to the BOLD fMRI response to somatosensory stimulation in rats

Y. Hirano[1], and A. C. Silva[1]

[1]Cerebral Microcirculation Unit, Laboratory of Functional and Molecular Imaging, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, United States

Introduction: Biophysical models of BOLD contrast have assumed that the arterial vasculature is fully saturated with oxygen [1-2], so that BOLD originates in the capillary network and the venous side of the vasculature. Recently, optical imaging experiments coupled with direct PO_2 measurements have shown a significant loss of oxygen from large arteries to arterioles in the cerebral cortex, and that the largest fractional increases in oxygenation upon functional activation occur in the arterial side of the vasculature [3]. The main implication to fMRI is that a measurable fraction of the BOLD response may have an arterial origin. Here, we measured the BOLD and CBF fMRI response to somatosensory stimulation in α-chloralose anesthetized rats under different levels of arterial oxygenation to examine the arterial contribution to BOLD.

Materials and Methods: Adult Sprague-Dawley rats (n=6, 298±40g) were orally intubated and anesthetized with α-chloralose. fMRI experiments were performed in a horizontal 7T/30cm magnet equipped with a 15cm gradient coil. Images were acquired using a home-built transmit volume coil and a receive surface coil. A dedicated labeling coil was placed in the neck region for ASL. Simultaneous BOLD and CBF-fMRI was performed using dynamic ASL (DASL) sequence [4] with the following parameters: TE=25ms, TR=250ms, flip angle=30°, matrix size=64×64, in-plane resolution=400×400mm^2, slice thickness=2mm, acquisition bandwidth=170kHz. A pair of needle electrodes was inserted into each forelimb and bilateral forepaw stimulation was accomplished by paired electrical stimulation (333μs pulses, 2mA amplitude, 3Hz) for 4s in each 30s epoch. The fraction of inspired oxygen (FiO_2) was varied between 21% and 40% in different fMRI sessions. Arterial blood gasses were sampled periodically during experiments. Moderate hypoxia, normoxia and hyperoxia states were defined for each animal based on the measured PaO_2. Region-of-interest analysis of the BOLD and CBF responses to somatosensory stimulation was performed.

Results: PaO_2 were 71.3±11.3, 98.6±8.8 and 144.3±21.4mmHg in hypoxia, normoxia and hyperoxia, respectively. Robust BOLD (Fig. 1A) and CBF (Fig. 1B) responses were obtained in all conditions. The BOLD response to somatosensory stimulation obtained in normoxia had the highest peak amplitude, while the responses obtained during normoxia and hyperoxia were smaller (Fig. 1A). On the other hand, the amplitudes of the CBF responses to normoxia or hypoxia were similar, slightly higher than that of the response to hyperoxia (Fig. 1B). Hypoxia caused a significant delay in the onset-time (OT) and time-to-half-maximum (THM) of the BOLD response compared to normoxia (Fig. 2A-B, $p < 0.05$), but the times-to-peak (TTP) under all conditions were similar (Fig. 2C). On the other hand, the different levels of arterial oxygenation had no effect on the CBF OT, THM and TTP (Fig. 2), which were all significantly shorter than their respective BOLD counterparts (Fig. 2, $p < 0.05$). Relative to normoxia and hyperoxia, hypoxia significantly increased the OT difference between CBF and BOLD (Fig. 2A), indicating a significant delay in onset of BOLD.

Discussion: Moderate hypoxia affected neither the amplitude nor the OT of the CBF response to somatosensory stimulation, suggesting that the CBF response is not critically dependent on the level of arterial oxygenation. Interestingly, under normoxia and hyperoxia, the OT difference between CBF and BOLD (~150ms) is significantly shorter than the arteriole-venule transit-time (~0.5s) [4], suggesting that at least some small fraction of the BOLD response comes from the arterial side of the vasculature. Hypoxia significantly extended the BOLD OT, elongating the transit of oxygen across the vasculature. Based on the BOLD amplitude at 0.5s following stimulus onset, we estimate that the relative arterial contribution to the overall BOLD response is ~5%.

References: [1] Ogawa S et al., Biophys J. 1993 [2] Davis et al., PNAS 1998 [3] Vazquez AL et al., JCBFM 2010 [4] Barbier EL et al., MRM 2001, [5] Hutchinson EB et al., Neuroimage 2006.

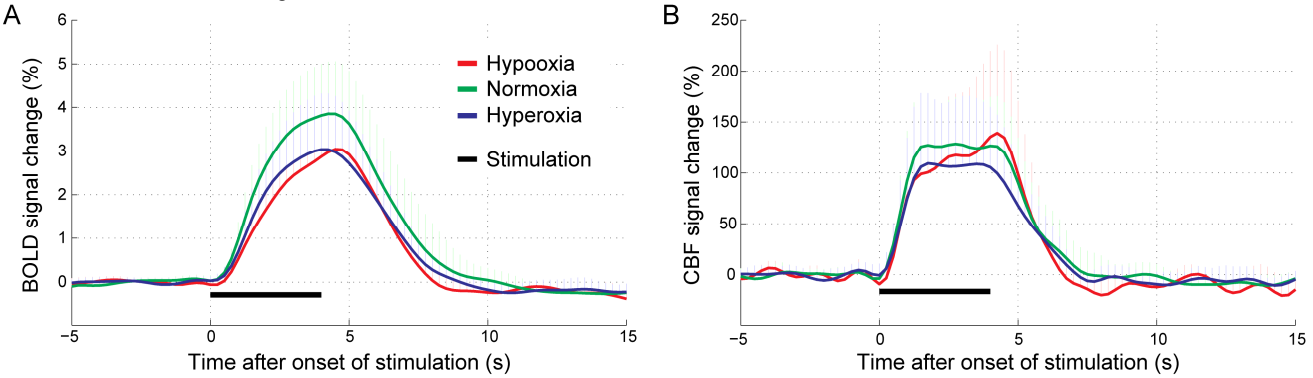

Fig. 1. BOLD (A) and CBF (B) percent signal changes to 4 s forepaw stimulation (black line) in S1 in hypercapnia (red), nomoxia (green) and hypercapnia (blue). Error bars show standard deviation.

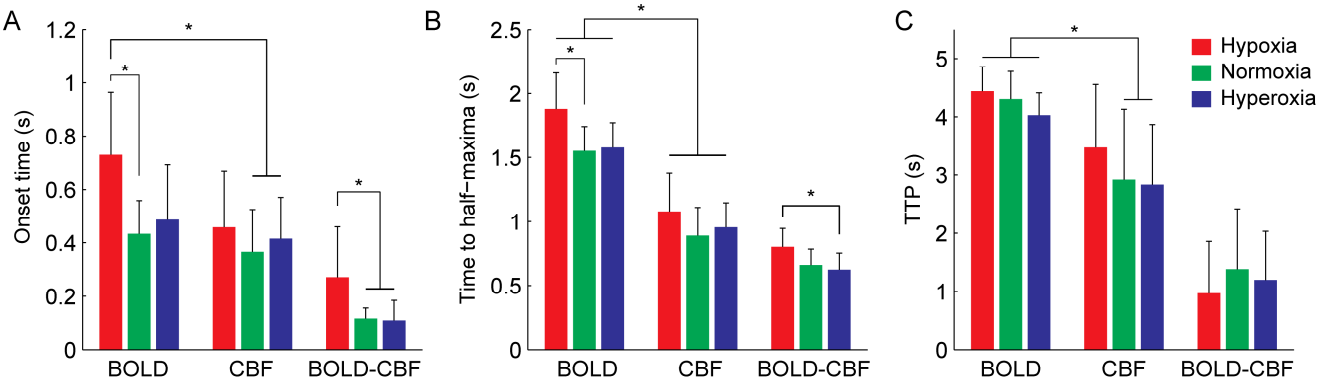

Fig. 2. Onset time (A), time to half-maxima (B) and TTP (C) of BOLD (left columns), CBF (center) and differences between BOLD and CBF in each session (right). Onset time and time to half-maxiuma of BOLD in hypocapnia were longer compared to that in normoxia (* $p < 0.05$).