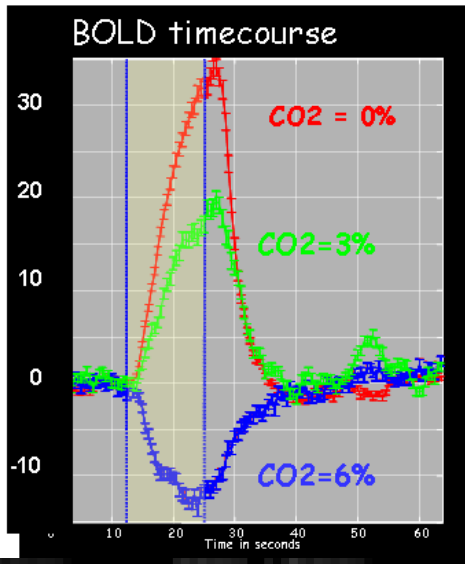
Negative BOLD signal under 6% hypercapnia reflects solely oxygen extraction from the blood

A-C. Zappe[1], K. Uludag[2], and N. K. Logothetis[1,3]

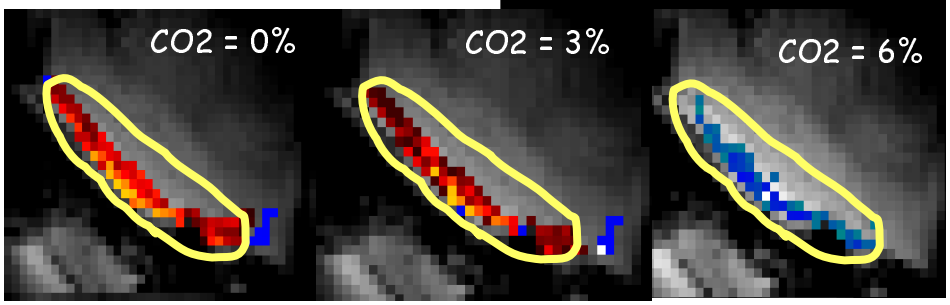
[1]Neurophysiology, Max-Planck-Institute for biological Cybernetics, Tuebingen, Baden, Germany, [2]High-Field MRI Center, Max-Planck-Institute for biological Cybernetics, Tuebingen, Baden, Germany, [3]Imaging Science and Biomedical Engineering, University of Manchester, Manchester, United Kingdom

Introduction: The BOLD signal is an indirect hemodynamic signal which is sensitive to cerebral blood flow (CBF), cerebral blood volume (CBV) and oxygen extraction fraction (OEF). Hypercapnia is often used as a vasodilatory challenge to calculate oxygen metabolism change during stimulation from combined CBF and BOLD data. In addition, it is used in clinical applications and basic research, and in mild to moderate concentration it does not impair function. In the current study, on anesthetized monkeys, negative BOLD responses to visual stimulation were observed for 6% CO2 in the majority of voxels responding positively during normocapnia. CBF and CBV did not respond to the sensory stimulation under 6% CO2. In contrast, the stimulus induced response magnitude of multi unit activity (MUA) and local field potentials (LFP) acquired simultaneously with fMRI data were not affected by any hypercapnia level. That is, the BOLD response under 6% inhaled CO2 to a sensory stimulus in anesthetized monkeys directly reflects oxygen extraction from the blood.

Methods: Combined electrophysiology and fMRI recording were performed in the primary visual cortex of 5 anesthetized monkeys in 8 experimental sessions using the techniques described by Logothetis et al in Nature 2001. Hypercapnia was induced by administration of premixed medical gases containing 3 % or 6 % CO2 and 21 % O2. Ventilation with 3 % and 6 % CO2 increased end-tidal CO2 by approximately 9 mmHg and 20 mmHg, respectively. For visual stimulation, a rotating full field checkerboard was presented to both eyes of the monkey (12s on/ 12s off/ 39s on). For analysis of the BOLD data, an ROI has been selected at normocapnia restricted to V1 and correlation coefficients larger than 0.15.



Results During normocapnia, the ROI in V1 contained in average 120±60 voxels with a positive correlation coefficient. During 3% CO2 the amplitude of the BOLD response decreased and only few voxels (5±5) were negatively correlated to the paradigm. During 6% CO2 most active voxels within the ROI (70±40) were negatively correlated. Importantly, the amplitude of the stimulus-induced responses of MUA and LFP responses during stimulation remained stable during both 3 and 6% CO2 compared to normocapnia. CBF or CBV acquired in different sessions did not respond to stimulation for 6% CO2 (data not shown).



Conclusions The BOLD signal during 6% hypercapnia can be used to investigate the cerebral metabolic rate of oxygen consumption (CMRO2) without the concomitant changes in CBF and CBV while the electrophysiological responses were preserved. With this method, oxygen extraction can be imaged by means of fMRI without injection of an exogenous drug such as sodium nitroprusside which has been used for similar purpose in the cat [3]. In our lab, it has been found that sodium nitroprusside, however, does not achieve a ceiling of CBF and CBV in the macaque monkey as observed in this study during 6% hypercapnia.

[1]Logothetis at al. Nature (2001); [2] Logothetis et al. NatNeurosci (1999); [3]Fukuda et al. NeuroImage (2006).