Calibrating the BOLD signal revisited – Calculation of oxygen metabolism for gradient- and spin-echo sequence up to 16.4T

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Introduction

The baseline fMRI signal and the blood oxygenation level-dependent (BOLD) signal amplitude are not a quantitative reflection of neuronal activity as physiological and physical parameters (e.g. baseline CBF, echo time, coil sensitivity …) contribute to the the signal. One goal of quantitative fMRI is to determine oxygen metabolism ($CMRO_2$) from fMRI data. To this end, a calibrated BOLD approach has been proposed calculating oxygen metabolism from combined CBF and BOLD data [1,2]. The calibrated BOLD approach for GRE sequence at 1.5T has been derived under the assumption that only extra-vascular signal from mostly veins contributes to the BOLD signal. Recently, we have proposed an alternative model, named the 'integrative model' which takes into account intra- and extra-vascular contributions of micro- and macro-vasculature for both GRE and SE up to 16.4T [3]. Using the integrative model, a general calibration model of the BOLD signal as a function of oxygen extraction fraction (OEF) and total CBV is derived and applied, for the first time, on 7T GRE and SE fMRI data obtained on the macaque monkey.

Methods

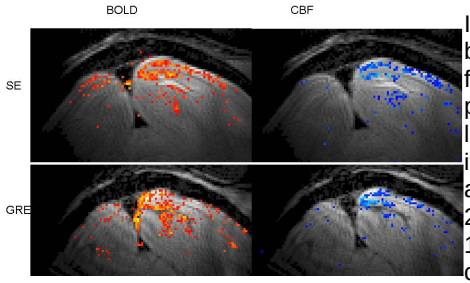
For simplicity, the total BOLD signal as calculated from the integrative model [3] for GRE respectively for SE is fitted with a first order equation, which is our main equation to determine $CMRO_2$ (see table for macro-vasculature):

$$\frac{\Delta S}{S} = B^{(*)} \cdot \left(\frac{\Delta Y_v}{Y_{0v}} - g^{(*)} \cdot \frac{\Delta v}{v_0} + i^{(*)} \cdot \frac{\Delta Y_v}{Y_{0v}} \cdot \frac{\Delta v}{v_0} \right)$$

field [T]	g	i	g*	i*
1.5	-0.125	0.998	0.353	0.861
3	0.330	0.996	0.405	0.803
4	0.415	0.994	0.430	0.767
4.7	0.452	0.992	0.434	0.748
7	0.533	0.987	0.442	0.697
9.4	0.594	0.980	0.425	0.666
11.7	0.642	0.974	0.409	0.638
14.1	0.686	0.968	0.393	0.611
16.4	0.726	0.962	0.376	0.583

Note that the BOLD signal is not only a function of relative oxygenation change $\frac{\Delta Y_v}{Y_{0v}}$ (in venules or veins) and relative total volume change $\frac{\Delta v}{v_0}$ but also of the product of these changes. The terms g and i are parameters empirically fitted to the BOLD signal amplitudes derived from the integrative model and the asterisk * label the values for GRE. The term B is a scaling constant which can be determined from a hypercapnia experiment analogously to the previous calibrated BOLD approach [1]. We apply this model to high-resolution monkey data acquired at 7T with continuous arterial spin labeling with both GE and SE using the following parameters: 8-segment multi-slice images with 500x500x2000μm^3. TR = 3s, TE = 12/30ms (GE/SE), labeling time = 2s, delay = 800ms, 3% CO_2 given for one minute followed by 8 cycles of 12s rest and 12s visual stimulation.

Results



In the Figure, functional activation is shown overlaid on the averaged EPI image. As can be seen, BOLD signal activation at 7T using SE is primarily located in the tissue whereas for GRE, the BOLD signal has its maximum at the brain surface as shown already in previous studies and predicted by the integrative model (see [3] for references). The largest CBF change is also in tissue layers for both SE and GRE acquisitions as expected if the transit delay of tagged blood is taken into account by the ASL imaging scheme. The amplitude of CBF and BOLD changes during hypercapnia and stimulation were for SE: 26% and 1.6% for hypercapnia and 105% and 1.94% for stimulation, and for GRE: 11.49% and 1.15% for hypercapnia and 137% and 2.40% for stimulation. Using the current model, *n* values (ratio of fractional CBF and $CMRO_2$ changes) 2.77 and 2.88 were obtained for GE and SE respectively.

Discussion

In this study, we developed a BOLD signal model as a function of oxygen extraction fraction and CBV in order to determine oxidative metabolism change from combined BOLD and CBF data. The new model is an alternative model to the widely used calibrated BOLD approach initially proposed by Davis and colleagues for GRE at 1.5T [1]. In contrast to the Davis' model, the new model takes also intra-vascular MRI signal into account and is developed for both GRE and SE up to 16.4T [3]. In the current study, oxidative metabolism change during visual stimulation was determined in macaque monkeys at 7T using SE and GRE. Note that the calibrated BOLD approach was never applied before neither using SE, at 7T nor in macaque monkeys. It was found that the coupling constant n lies between 2.77 and 2.88 in agreement with previous MRI and PET results (overview of some of these results, see [4,5]). Furthermore, published data using the calibrated BOLD approach at 1.5T, 3T and 4.7T were re-analyzed using the new model (data not shown). As a result, slightly lower average n-values 2.58±0.83 were obtained compared to the value of 2.72±0.89 using the Davis' model. In summary, a new calibrated BOLD approach was presented which is more general than the previous model as it is valid up to 16.4T and it has been also developed for SE. Results for oxygen metabolism were consistent at different field strengths for both GRE and SE.

References

[1] Davis et al., PNAS (1998) [2] Hoge et al., MRM (1999) [3] Uludag et al., NeuroImage (submitted) [4] Gjedde et al., JCBFM (2002) [5] Leontiev et al., NeuroImage (2008).