

High resolution CMRO₂ in visual cortex of macaca mulatta

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Introduction

Current fMRI-methods are based on changes in cerebral blood flow and/or oxygenation. Since these methods measure a hemodynamic signal, changes in BOLD or CBF may not always accurately reflect changes in the actual energy use of the brain. Particularly in disease-states or in pharmacological MRI it may be difficult to disentangle the contribution of the vascular system and neural energy consumption. Measuring CMRO₂ allows one to determine if differences in hemodynamic signals are caused by underlying changes in neural function or whether these are due to vascular effects. Therefore, being able to accurately measure CMRO₂ is advantageous, especially when it can be measured at high resolution. Increasing resolution means reducing partial volume effects and allows an accurate determination of CMRO₂ in gray matter. In this study, we used calibrated BOLD to determine CMRO₂ in anesthetized macaques at high field at a resolution of 1x1x3 mm³.

Methods

Experiments were performed on a vertical 7T scanner (Bruker BioSpec 70/60v) in one anesthetized monkey (*macaca mulatta*) weighing 9 kg. The setup and methods have been described previously [1,2]. Anesthesia was a balanced remifentanyl/mivacurium regimen. End-tidal CO₂ was monitored and maintained within normal range. The visual stimulus was a full-field rotating checkerboard alternating with blank periods (block design with 72s periods on-off, 128 images). The hypercapnic challenge consisted of 3 min 12s baseline, 8 min 3% CO₂ gas mixture inhalation and another 10 min 3s baseline period. CBF and BOLD data were acquired simultaneously with a triple-echo sequence [3] at a resolution of 1x1x3 mm³, using a TR of 4.5s, TI of 1125 ms/1400ms and TE of 6.6ms/23.4ms. CBF and BOLD percentage changes were calculated in a ROI in V1 and V2 defined based on a clustered CBF activation map. M and CMRO₂ values were calculated voxel-by-voxel using the calibrated fMRI model [4,5] with $\alpha=0.38$ and $\beta=1.5$. Voxels had to be significantly activated in all functional maps to be included in the calculation. Mean M and CMRO₂ percentage change values were obtained by averaging over the ROI. We also calculated the ratio of fractional CBF and CMRO₂ changes (n).

Results

Figure 1 shows functional activation maps during visual stimulation and hypercapnia overlaid on their respective baseline EPI images. During visual stimulation, CBF increased by 30.8±15.5% (mean ± SD) and BOLD by 3.6±1.7%. Hypercapnia induced a change of 17.7±11.7% in CBF and 2.8±1.1% in BOLD. The average M value within the ROI was 0.26±0.09. Figure 2 shows the CMRO₂ percent change map, indicating the CNR was sufficient to allow for high-resolution CMRO₂ measurement. The change in CMRO₂ upon visual stimulation, averaged over the ROI was 9.8±3.0%. The coupling constant n was 3.15.

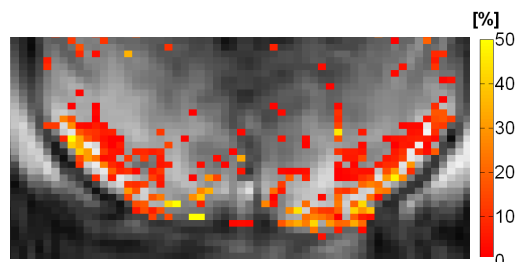


Figure 2: CMRO₂ map

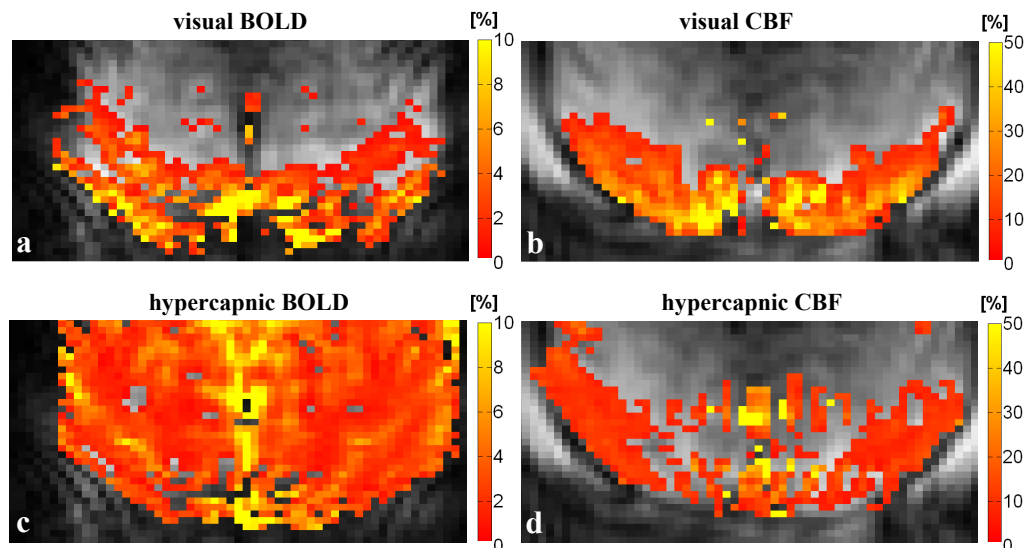


Figure 1: visual (a: BOLD, b: CBF) and hypercapnic (c: BOLD, d: CBF) activation maps

Conclusion

Robust high resolution CBF and BOLD maps were acquired at high field during visual stimulation and hypercapnia, which allowed for calculation of the CMRO₂ map. BOLD- and CBF changes associated with visual stimulation were in the range of values typically obtained in anesthetized macaques [6], and CMRO₂ values were consistent with those reported in humans [4,7] and anesthetized baboons [8]. The coupling constant n is in agreement with previous MR and PET results such as reviewed in [7]. In conclusion, we showed that high resolution CMRO₂ can be determined in macaques. In future, this approach may be used in combination with electrophysiological or pharmacological interventions to gain further insights in the brain energy metabolism.

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References: [1] Goense et al., MRI 28: 1183-1191 (2010); (2010); [2] Logothetis et al., Nat Neurosci 2: 555-562 (1999); [3] Yang et al., MRM 52: 1407-1417 (2004); [4] Davis et al., PNAS 95: 1834-1839 (1998); [5] Hoge et al., MRM 42: 849-863 (1999); [6] Zappe et al., JCBFM 28: 640-652 (2008); [7] Leontiev et al., NeuroImage 36:1110-1122 (2007); [8] Wey et al., JCBFM in press