Calibrated fMRI using simultaneous EEG and fMRI and the effect of hypercapnia on CMRO2

A. Federspiel[1], A. Orosz[1], M. Hauf[2], R. Wiest[2], D. J. Wang[3], T. Dierks[1], and K. Jann[1]
[1]Department of Psychiatric Neurophysiology, University Hospital of Psychiatry, Bern, Switzerland, [2]Institute of Diagnostic and Interventional Neuroradiology, University of Bern, Switzerland, [3]Department of Neurology, UCLA, Ahmanson-Lovelace Brain Mapping Center, Los Angeles, CA, United States

Introduction: In the human brain increases in neuronal activity are at least accompanied by changes in cerebral blood flow (CBF), blood volume (CBV) and oxygenation (CMRO2). These changes can be measured via blood oxygenation level dependent (BOLD) contrast mechanism [1, 2]. Unfortunately, the BOLD signal does not allow disentangling these entities: calibrating the BOLD signal is therefore indispensable. Carbon dioxide (CO_2) is used as a vasodilator to estimate changes in CMRO2. Through the measure of CBF using arterial spin labeling (ASL) [3-6] and through Grubb's relation between CBF and CBV, the necessary conditions for establishing the relationship between changes on BOLD, CBF and CMRO2 and M [7] are given. One basic assumption in this model is that under moderate hypercapnia CMRO2 is not altered. Recently, this assumption was explicitly tested [8, 9]. In the later work electroencephalography (EEG) was measured, not on the same acquisition setup however. Some findings showed an local field potential (LFP) effect in beta and gamma band during hypercapnia [10], others did not [11]. In summary, an unambiguous consensus does still not exist about the basic assumption of whether during hypercapnia the fractional CMRO2 remains constant. This leads to the following hypothesis of the present investigation: within the same subject and the same recording setup, during resting state no changes in EEG will be observed under hypercapnia.
Methods: One single female subject participated in the Pilot study (age 27.4 years). The imaging session consisted of ASL- and BOLD scans: 1) hypercapnia (HC) scan with inhalation of 7% CO_2 gas mixture through a nonrebreathing face mask (2 min room air, 3 min 7% CO_2, 2 min room air) and 2) a block design functional scan [visual stimulation; see below] with room air (NA) (2 min off, 6×(30 s on/30 s off), 2 min off). During all these functional scans, simultaneous EEG recording inside the scanner was performed. Visual stimulation of a 2 Hz full-field flashing checkerboard pattern with a small white fixation cross in the center. ***Anatomical scan*** (MDEFT) [12] followed by ***fMRI scan*** T2*-weighted gradient echo planar imaging TE/TR [ms]=30/3000,FA=90º,32 axial slices, slice thickness (ST)=4 mm, gap=0 mm, FOV=240 mm, matrix=64 x 64. In total, 156 volumes were collected during HC scan, and 208 volumes were collected during NA scan. ***ASL scan*** using pseudocontinuous ASL (pCASL) sequence [13, 14] with 8-channel head coil FOV=220 mm, matrix=64 x 64, axial slices=5, ST=8 mm, gap=1.5 mm, TE/TR[ms]=17/3000, slice-selective gradient = 6 mT/m, tagging duration τ = 700 ms and postlabeling delay (w) = 1000 ms. In total, 156 volumes were collected during HC scan, and 208 volumes were collected during NA scan. ***EEG recording*** using a 92 channel (5 kHz sampling rate, 16.3mV input range, bandpass filter 0.1-250 Hz, impedance below 20 kΩ; BrainAmp MR, Brain Products, Gilching, Germany). EEG was recorded first outside scanner (6 minutes) and then inside the scanner for simultaneous EEG-fMRI acquisition. Calculation of M and CMRO2 was according to 'Davis-Model' [7].
Results: End-tidal CO_2 increase of 6 mm Hg during HC. Heart rate (HR) increase of 7 units during HC. Whole brain resting perfusion [in gray matter] CBF = 45.63 [ml/100g/min] and increase to 58.80 [ml/100g/min] during HC. ROI extraction provided CO_2 runs: BOLD (%): 0.71 ± 0.87, CBF (%): 26.86 ± 7.40. Calculation of M=5.02 ± 15.56. Calculation of CMRO2 (Stimulus-induced runs: BOLD (%): 0.48 ± 0.72, CBF (%): 13.57 ± 9.72) yielded CMRO2 change (%) =5.62 ± 0.05. Alpha power decreased during HC. The results are shown in the figures. Visual evoked potentials showed latency of P100 peak at 116 ms. Estimation of current density during HC localized in the early visual cortex [15]. During HC a reduced power in frequency bands theta and alpha 2 are observed. In beta power frequency an increase is observed during HC.

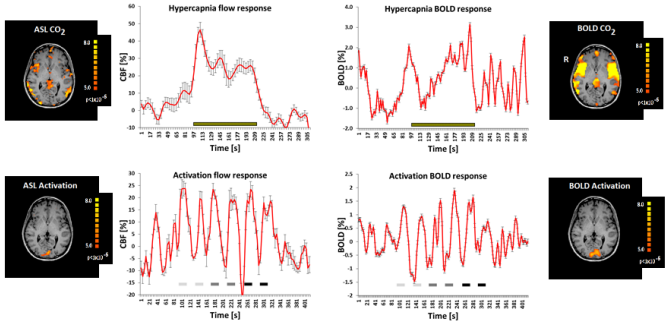

Figure 1: SPM maps showing the region of activation evoked by visual stimulation. Time course of %CBF and %BOLD during hypercapnia (above) and during visual stimulation (below) are extracted from ROI of the ASL GLM analysis. P-threshold for all images $p<1x10^{-6}$ (FDR-corrected) [T-value>5.0].

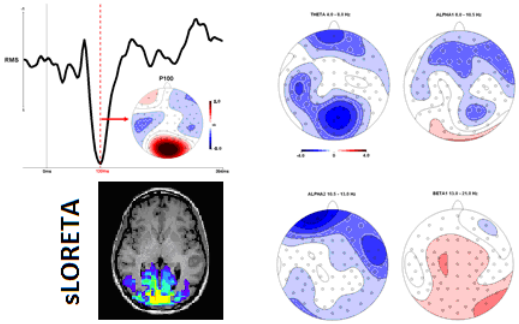

Figure 2: Global field potential and P100 map of the visually evoked responses averaged across all trials during BOLD scan (artifact corrected, average reference, no baseline correction).Corresponding current density estimation (sLORETA). T-test of EEG spectra during CO_2 and AIR shows decreased theta and alpha2 power during CO_2 [blue-color].

Conclusions: The present Pilot study shows values of CBF, M and CMRO2 that are in line with previous findings [8, 9,16,17]. The observed reduction in alpha power could indicate that CMRO2 under CO_2 administration does not remain constant. A relation between changes in CMRO2 and frequency of a neuronal cluster was suggested earlier [18]. The present findings are in line with previous observations tested [9], but at odds with other findings [8]. Only an extension of the present Pilot study with more measurements can clarify whether the basic assumption of the method used in calibrated fMRI can hold. These future findings will clarify the influence of hypercapnia to CMRO2, as the measure will be obtained within the same subjects and within the same multimodal recording scheme.

References:

[1] Ogawa, S., et al., Magn Reson Med, 1990. 14(1): p. 68-78. **[2]** Bandettini, P.A., et al., Magn Reson Med, 1992. 25(2): p. 390-7. **[3]** Brown, G.G., et al., J Cereb Blood Flow Metab, 2003. 23(7): p. 829-37. **[4]** Wong, E.C., J Magn Reson Imaging, 2005. 22(6): p. 727-31. **[5]** Detre, J.A. and J. Wang, 2002. 113(5): p. 621-34. **[6]** Wang, J., et al., Magn Reson Med, 2003. 50(3): p. 599-607. **[7]** Davis, T.L., et al., Proc Natl Acad Sci U S A, 1998. 95(4): p. 1834-9. **[8]** Chen, J.J. and G.B. Pike, J Cereb Blood Flow Metab, 2010. 30(6): p. 1094-9. **[9]** Xu, F., et al., J Cereb Blood Flow Metab, 2010. **[10]** Zappe, A.C., et al., Cereb Cortex, 2008. 18(11): p. 2666-73. **[11]** Jones, M., et al., Neuroimage, 2005. 27(3): p. 609-23. **[12]** Deichmann, R., et al., Neuroimage., 2004. 21(2): p. 757-767. **[13]** Dai, W., et al., Magn Reson Med, 2008. 60(6): p. 1488-97. **[14]** Wu, W.C., et al., Magn Reson Med, 2007. 58(5): p. 1020-7. **[15]** Pascual-Marqui, R.D., Methods Find Exp Clin Pharmacol, 2002. 24 Suppl D: p. 5-12. **[16]** Ances, B.M., et al., Neuroimage, 2008. 39(4): p. 1510-21. **[17]** Chiarelli, P.A., et al., Magn Reson Med, 2007. 57(3): p. 538-47. **[18]** Hyder, F., Stroke, 2004. 35(11 Suppl 1): p. 2635-41.