Regional quantification of cerebral venous oxygenation from MRI susceptibility mapping during hypercapnia

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Target audience. Physicians and scientists interested in noninvasive imaging of venous oxygenation in the brain.

Purpose. To validate regional measurements of oxygen extraction fraction (OEF) derived from quantitative susceptibility estimates in individual cerebral veins [1]. Since an elevated level of end-tidal carbon dioxide ($ETCO_2$) is known to cause a decrease in oxygen extraction [2], we measured OEF during eucapnia and moderate hypercapnia conditions as a proof-of-concept study in healthy subjects. Regional changes in perfusion were used to predict local oxygenation changes and compared with quantitative susceptibility mapping (QSM)-based OEF estimates in veins draining the cingulate, occipital, parietal, and frontal cortices.

Methods. _Gas experiments_. Eight healthy volunteers (ages 24-31 years) were scanned with a 32-channel coil on a Siemens 3T Trio system. $ETCO_2$ was monitored continuously in each subject with a capnograph (CWE Inc., Capstar-100). After acquisition of structural T_1-weighted images, subjects breathed on a circuit [3] designed to maintain stable $ETCO_2$. Inspired gases were adjusted to achieve steady-state levels of eucapnia (42±3mmHg) and hypercapnia (51±3mmHg). Gradient echo (GE) images for susceptibility mapping and pseudo-continuous arterial spin labeling (PCASL) images were acquired during each breathing condition. The 3-dimensional GE scans were flow-compensated along all axes [4] with $TR/TE_1/TE_2$=23/7.2/17.7ms; resolution=0.875x0.875x1.0mm^3; matrix=256x224x224; TA~6min. The PCASL scans were collected with TR/TE=3500/13ms; resolution=3.4x3.4x6mm^3; 40 control-tag pairs; 1.5ms label delay; 1.2s post-label delay; TA~5min; and a separate scan for M_0 calibration. _OEF prediction and estimation._ FreeSurfer cortical segmentation [5] was performed on the anatomical scans and PCASL CBF was assessed for selected cortical ROIs. Assuming no change in the cerebral metabolic rate of oxygen ($CMRO_2$) [6], we predicted the OEF decrease from hypercapnia as $\Delta OEF=(CBF_E/CBF_H-1)\cdot OEF_E$, where E=eucapnic and H=hypercapnic states. Phase images were spatially unwrapped, background field was removed with dipole fitting [7], and QSM maps were reconstructed with use of a magnitude prior for regularization [8]. $OEF=1-\Delta\chi_{vein\text{-}CSF}/(4\pi\cdot\Delta\chi_{do}\cdot Hct)$ was quantified in individual vessels [9] draining the cingulate, occipital, parietal, and frontal cortices (***Fig1***). Here $\Delta\chi_{do}$=0.27ppm and hematocrit (Hct) was measured in each subject (mean=42%, N=8).

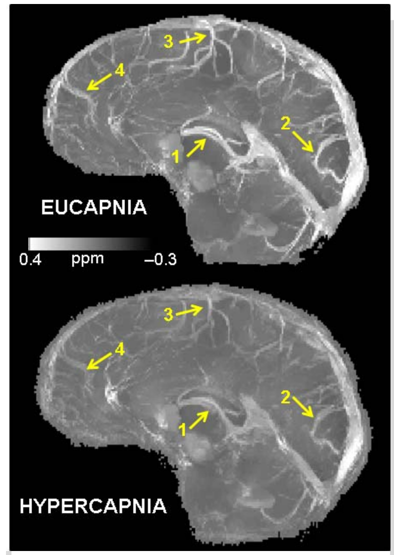

Fig1. QSM maps exhibit expected contrast change between gas states in veins of interest, indicated for (1) cingulate; (2) occipital; (3) parietal; and (4) frontal regions.

Results. Decreased vessel susceptibility contrast was observed on the QSM maps during hypercapnia compared to eucapnia (***Fig1***). Changes in CBF and OEF were correlated with the magnitude of change in $ETCO_2$, as shown in the cingulate cortex (***Fig2***). Mean absolute measurements of CBF and OEF across subjects are shown in ***Table1***; the percent change in CBF and OEF were similar in magnitude and consistent across regions. Measured versus predicted OEF decreases are shown for each region with a linear fit (***Fig3***). For each regression, we evaluated whether the slope was different from the expected value of 1, using a t-statistic = (fitted slope – 1) / (standard error of the slope). None of the t-statistics (cingulate=1.0, occipital=0.2, parietal=1.4, frontal=0.5) were significant at the 5% level.

Conclusion. Measured OEF changes during hypercapnia from MR susceptibility show good agreement with predictions based on regional flow observations and no change in $CMRO_2$, and suggests that regional estimates of OEF in vessels from QSM maps are reliable.

[1] Fan *MRM* (2013) doi:10.1002/mrm.24918. [2] Jain *JCBFM* 2011. [3] Banzett *J Appl Physiol* 2000. [4] Deistung *JMRI* 2009. [5] Dale *Neuroimage* 1999. [6] Liu *NMR Biomed* 2011. [7] Chen *JCBFM* 2010. [8] Bilgic *MRM* (2013) in press. [9] Haacke *HBM* 1997. **Funding**: NBIB T32-EB001680.

Region	Eucapnia	Hypercapnia	% Change
Cerebral Blood Flow – CBF (ml/100g/min)			
Cingulate	48.4 ± 4	76.5 ± 9	58 ± 14
Occipital	49.5 ± 3	71.5 ± 10	45 ± 19
Parietal	40.2 ± 3	56.2 ± 6	40 ± 12
Frontal	46.6 ± 4	71.8 ± 6	54 ± 18
Oxygen Extraction Fraction (%)			
Cingulate	29.9 ± 7	15.7 ± 5	47 ± 9
Occipital	25.9 ± 3	11.7 ± 2	54 ± 8
Parietal	29.3 ± 6	13.6 ± 3	53 ± 7
Frontal	31.3 ± 6	14.4 ± 3	53 ± 8

Table1. Mean and standard deviation of measured CBF and OEF in each gas state (N=8).

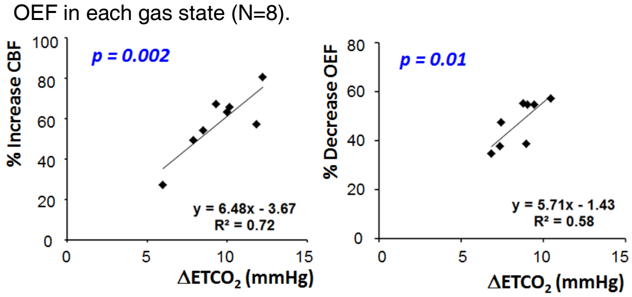

Fig2. Measured percent change in CBF and in OEF versus change in $ETCO_2$ across volunteers for the cingulate cortex.

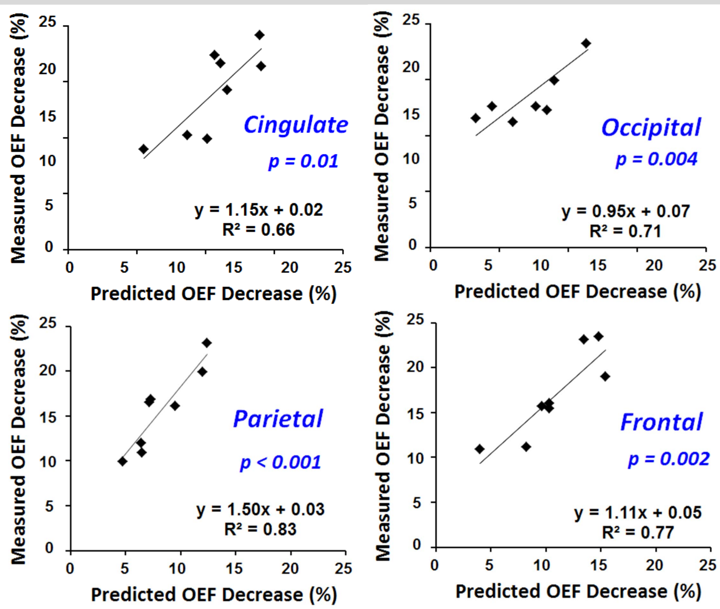

Fig3. Measured OEF decrease versus predicted OEF decrease across volunteers, shown in four cortical regions. The R^2 values indicate goodness-of-fit for the linear regression, and the measured slope for each region was not different from the expected slope of 1 by t-statistic.