

Feasibility of Estimating CBF/CMRO₂ Coupling with a Calibrated-BOLD Method When the Driving Stimulus is Unknown

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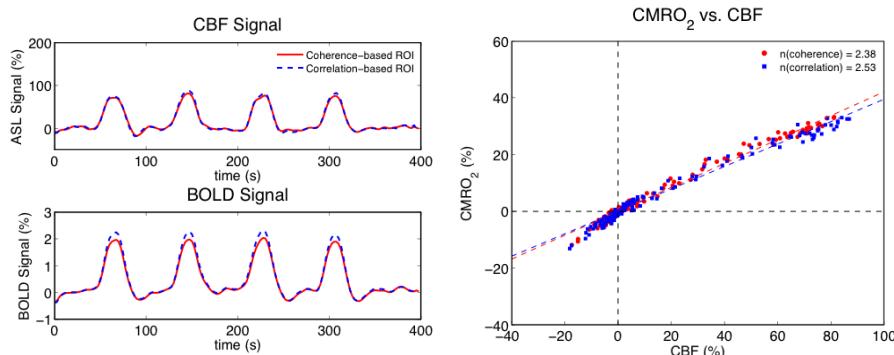
Purpose

The calibrated-BOLD method [1] provides a way to measure the coupling of cerebral blood flow (CBF) and the cerebral metabolic rate of O₂ (CMRO₂) during brain activation. To date, this method has been applied to studies with well-defined stimuli presented in a simple block design (with the exception of [2]). For region of interest (ROI) analysis, ROI's typically are chosen based on voxel time course correlation with the known stimulus pattern. In this study we tested the feasibility of using just the coherence of the CBF and BOLD signals measured simultaneously with a dual echo spiral ASL technique, with no prior knowledge of the stimulus itself, as a way to identify signal variations associated with brain activity. This approach would make possible the assessment of CBF/CMRO₂ coupling with more complex stimuli where a model response is not known, and would provide a basis for a wider application of this method as a probe of disease.

Methods and Results

A novel *CBF/BOLD-coherence* analysis was compared with the standard *model-correlation* analysis for deriving ROI-based curves of CBF and BOLD responses for estimation of CMRO₂ changes based on the calibrated-BOLD method [1].

Experimental data and preprocessing. Image data from 8 healthy, adult subjects was obtained from a previous study at 3T of CBF/CMRO₂ coupling during visual stimulation based on simultaneous dual-echo acquisition of CBF and BOLD signals [3]. Each functional run consisted of a 60s rest period followed by four 20s task/60s rest cycles and a final 30s rest period. A CBF time series was computed for each subject by taking the temporal surround-subtraction of the tag-control image series from the first echo data, and a BOLD signal time series was computed by taking the surround average from the second echo data [4]. Before analysis, nuisance parameters, including constant, linear, and physiological terms based on cardiac and respiratory monitoring, were removed from each time series using a general linear model (GLM) approach.



with high r-values, and took the intersection of these two maps as the model-correlation based ROI. An ROI with an equal total number of voxels (49.63 ± 18.77 voxels across subjects) was then constructed with the CBF/BOLD-coherence approach by correlating the CBF and BOLD time series and taking the same number of highest correlation voxels. The two ROI's did not completely overlap, but the ROI-averaged BOLD and CBF response curves were quite similar (left Figure: average curves across 8 subjects). From these curves the change in CMRO₂ was calculated for each time point, based on the Davis model [2] and plotted against the corresponding CBF change (right Figure: curve constructed from data in left Figure). The inverse slope of this curve was taken as an estimate of the CBF/CMRO₂ coupling index *n*, the ratio of the fractional CBF and CMRO₂ changes. A small but significant increase in BOLD response in correlation-based vs. coherence-based ROIs was found, and this difference was also reflected in a slight difference in the estimates of *n*: 2.57 ± 0.20 vs. 2.39 ± 0.25 (mean \pm sem) for correlation-based compared with coherence-based ROIs.

Discussion and Conclusions

This initial test supports the feasibility of a novel approach for identifying brain activation based on coherence of the CBF and BOLD signals, with no prior assumptions about the time course of the driving stimulus, by demonstrating that the estimates of CBF/CMRO₂ coupling are similar to those based on the standard model-correlation approach when the stimulus is known. This result supports two future applications of the calibrated-BOLD method: 1) as a quantitative tool to test whether CBF/CMRO₂ coupling is different with more natural stimuli than with the highly focal stimuli used to date; and 2) as the basis for measuring CBF and CMRO₂ responses to complex stimuli as a probe of disease.

1) Davis, PNAS 95:1834,1998; 2) Fukunaga JCBFM 28:1377, 2008; 3) Perthen, Neuroimage 40:237,1998; 4) Liu, Neuroimage 24:207, 2005

Comparing analysis approaches. In order to derive comparable size ROI's with the two methods, we first performed the standard model-correlation approach by constructing separate maps of the correlation coefficient between the model function (a smoothed version of the known block design of the stimulus) with the CBF and BOLD responses, identified the top 150 voxels with an algorithm designed to select clusters of voxels