Reducing inter-voxel variability of the BOLD response with measurement of resting blood flow

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Introduction

The blood oxygenation level-dependent (BOLD) signal used in functional magnetic resonance imaging (fMRI) is dependent on regional differences on the cerebral blood flow (CBF), cerebral blood volume (CBV), and oxidative metabolism. Previous studies have attempted to account for the regional differences in the intensity of the BOLD response by hypercapnic normalization[1,5]. In particular, [1] showed that normalized BOLD signal induced by a motor task was consistent across different magnetic fields and pulse sequences. However, hypercapnic normalization involves the delivery of $C0_2$ and may be difficult to implement for select clinical subject populations. Here we investigate the use of resting CBF as a possible alternative normalization technique by first examining the dependence of the functional BOLD response on resting CBF.

Methods

Experimental Protocol: A visual stimulation study was performed on 4 subjects with the use of a black and white radial checkerboard flashing at 8 Hz presented in a block design paradigm consisting of 4 cycles of 20s stimulation with 40s rest. An additional three minute resting scan was acquired for resting CBF quantification. Scanning was performed on a 3T GE Signa whole body system, with a body transmit coil and an 8 channel receive only head coil. A PICORE QUIPSS II [2] sequence was used with a dual gradient echo spiral readout. Imaging parameters for the visual stimulus were: TR=2s, TI1=600ms, TI2=1500ms, $\theta = 90°$, FOV = 24×24 cm2, matrix size 64×64, TE1=9.1ms, TE2=30ms, with four 7mm slices positioned through the primary visual cortex at an oblique angle parallel to the calcarine sulcus. The tagging band was 100 mm thick, positioned 10mm from the proximal edge of the first slice. A small diffusion pulse (b-factor=2) was also used. Cardiac pulse and respiratory effort data were recorded continuously with the use of a pulse oximeter and respiratory effort belt.

Image processing: Images from each subject were co-registered for motion correction. Perfusion (CBF) time series were formed from the running subtraction of the first echo. BOLD time series were formed from the running addition of the second echo. Cardiac and respiratory confounds were removed from the data using the methods described in [3]. ASL correlation maps were formed by correlating the CBF data with a reference function consisting of the stimulus pattern convolved with a gamma density function with nuisance parameters consisting of DC and linear trends. Functional localizer masks were formed by thresholding the ASL correlation maps at 0.3. A near-neighbor cluster threshold of one adjoining voxel was used to remove singletons. CBF values were quantified using cerebral spinal fluid (CSF) as a signal intensity reference [4] and averaged over time to obtain voxel-wise resting CBF values. The mean ($\hat{q}$) and standard deviation (σ) of the CBF values were computed for voxels within the functional localizer. The "Avg" flow bin was defined in the range ($\hat{q}$-σ/3)<CBF<($\hat{q}$+σ/3), with "High" flow defined by ($\hat{q}$+σ/3)<CBF<($\hat{q}$+σ), and "Low" flow in the range ($\hat{q}$-σ)<CBF<($\hat{q}$-σ/3). Time-series were then formed from the average across voxels within the functional localizer and for each of the three resting CBF bins. Paired t-tests were performed across subjects to determine the significance of changes in both the peak and post-stimulus undershoot amplitudes, time to 50% peak (rise-time), and full-width-half-maximum (fwhm).

Results

Figure 1 panels a) and b), show the group average CBF and BOLD responses binned according to the calculated resting CBF values. Error bars represent +- one standard deviation. With increasing resting CBF, the peak amplitude of the BOLD response increases significantly, with p-values equal to .017, .001,and .002 for comparisons between low-avg, low-high, and avg-high, respectively. There is also significant increases of the amplitude of the post-stimulus undershoot between low-high (p-value=.03) and avg-high (p-value=0.01) . However, there was no significant difference in the rise-time and the fwhm as a function of resting CBF. Additionally, there are no significant observed differences in the CBF response.

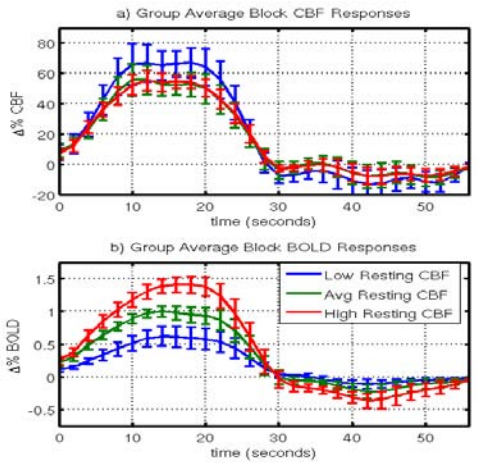

Figure 1.

Discussion

The BOLD signal change is weighted by the venous blood volume which is in turn a function of the resting blood flow. Consequently, we would expect the BOLD response to scale with increasing CBF without significant changes in the temporal characteristics. Here we show a clear relationship between resting CBF values and the amplitude of the BOLD response without changes in the dynamics. This result supports the use of resting CBF for the normalization of the BOLD response and the consequent reduction of inter-voxel variability.

References

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