Mapping functional connectivity in the anesthetized rat using CBV vs BOLD

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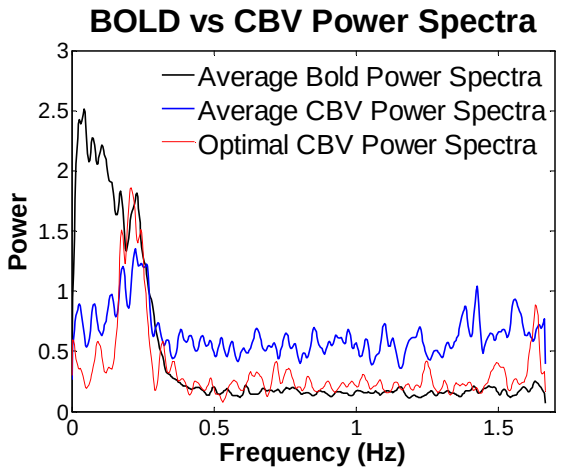
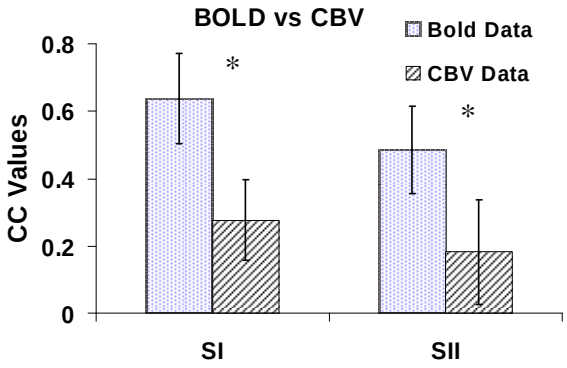
Introduction

Low frequency fluctuations in both blood oxygenation and cerebral blood volume (CBV) have been utilized to map functional connectivity in the rat [1, 2]. In previous studies it has been demonstrated that CBV-weighted fMRI is more sensitive and spatially accurate then BOLD fMRI for detecting somatosensory activation in the rat [3]. Few functional connectivity studies using CBV have been conducted [4] and no direct comparisons have been made between functional connectivity measurements made with CBV and BOLD in rats. In this study we compare cross correlation values and power spectral properties of CBV and BOLD fluctuations.

Materials and Methods

Five Sprague-Dawley male rats (250-350g) were imaged using a 9.4 T Bruker scanner (gradient strength of 20 G/cm, rise time 100 μs), with a two coil actively decoupled system, and anesthetized using medetomidine (bolus- .05mg/kg ; infusion- .1 mg/kg/hr). A single shot gradient-echo EPI sequence with TR = 300 ms (for RS scans) or TR = 1500 ms (for stimulation scans), TE=15 ms, field of view = 2.56 cm, and matrix size = 64 x 64 was used to acquire one 2mm slice centered over the primary somatosensory cortex. Three RS scans consisting of 1200 images (scan time 6 minutes 15 seconds) were acquired using the BOLD signal. Interleaved before each RS scan was a BOLD forepaw stimulation scan consisting of 180 images with 3 epochs of stimulation (30off–20on–30off–20on–30off–20on–30off). After all six of these scans were completed 2% isoflurane was administered for 1-3 minutes while paramagnetic iron oxide particles (Molday Ions, BioPal, Worcester, MA) were injected into the rat's tail vein through a previously placed catheter. The imaging paradigm described above was repeated. The primary somatosensory cortex (SI) was used as the seed region for power spectrum and cross correlation analysis. SI was identified by correlating a boxcar function representing the stimulation with the time course for the forepaw stimulation scan. The 15 pixels with the highest correlation values were defined as SI. Average power spectra were plotted for each ROI after linear detrending of the raw data. The center of mass for power in the low frequencies (BOLD 0.05-0.25 Hz; CBV 0.1-0.3 Hz) was determined. Cross correlation maps were obtained after the time courses were band-pass filtered to the frequencies of interest. T-tests were performed between the CBV and BOLD data for the center of mass and cross-correlation in SI and secondary somatosensory (SII).





Results and Discussion

Time courses from both BOLD and CBV data sets exhibit high power in the low frequencies and strong cross correlation between bilateral somatosensory areas (Fig. 1, top and bottom). BOLD power spectra show higher power in the very low frequencies (<0.1 Hz) as compared to CBV, which exhibits a much more localized peak (~.2Hz). For BOLD data sets the center of mass averaged .14 Hz while the center of mass for the CBV data sets averaged .21 Hz. The additional low frequency components of the BOLD signal may reflect contributions from metabolic oscillations in addition to the vascular oscillations presumably reflected in the CBV signal. All BOLD data sets showed strong bilateral connectivity in SI and SII; however the two earliest CBV data sets did not exhibit strong bilateral connectivity, possibly due to difficulties in iron oxide administration. Without these two CBV data sets, the cross correlation values in SI are .42±.008 (which remains statistically different from BOLD cross correlation) and the low frequency power spectrum has higher values within a narrower band (red plot in Fig. 1, top). The high temporal resolution in these scans prevents aliasing of the primary respiratory component of physiological noise; however, the TR was not sufficiently short to remove the primary cardiac component. However, the functional connectivity maps are qualitatively similar to maps obtained with a TR of 100 ms [1]. Despite the reduction of power in very low frequencies in the CBV signal as compared to the BOLD signal, cross correlation based on seeds in SI and SII produces similar connectivity maps for both. Future work will examine the contribution of the very low frequencies in the BOLD signal to functional connectivity maps. Multi-contrast MRI studies may provide insight into the relative metabolic and vascular contributions to low frequency fluctuations, leading to improved sensitivity to underlying neural activity.

References

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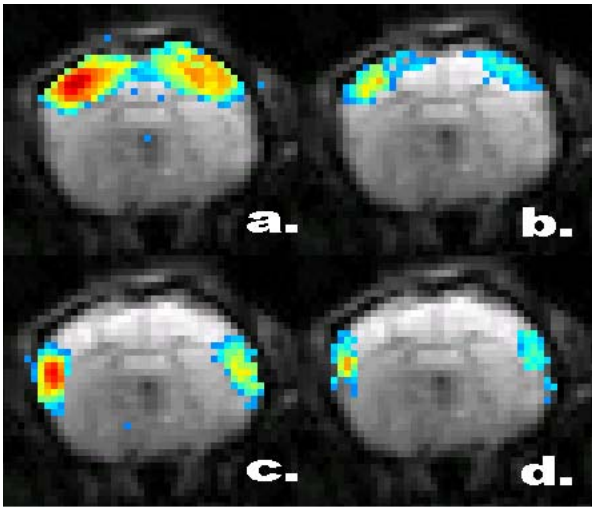

Figure 1: Top: Average Power spectra of BOLD and CBV scans. Red plot is the average CBV power spectra for the 5 'best' CBV scans. Middle: Average cross correlation values for each rat (* $p < .02$). Bottom: Typical BOLD (a,c) and CBV (b,d) cross correlation maps in SI (a,b) and SII (c,d) overlaid on the EPI image.