# CBF, BOLD and CBV Hemodynamic Coupling at 500-ms Temporal Resolution

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**Introduction** The tight coupling between hemodynamic and neural activity is the basis for many modern neuroimaging modalities. However, the temporal dynamics of the stimulus-evoked CBF and CBV responses and the resulting BOLD signals remain poorly understood and somewhat controversial. Silva *et al.* [1] reported a stimulus-evoked CBF onset of ~0.6s and it preceded the BOLD onset by ~0.5s in a rat forepaw stimulation model under α-chloralose anesthesia. Mandeville *et al.* [2] reported the CBV onset (measured using MION) was significantly delayed relative to the BOLD onset at 2 and 4.7T under α-chloralose anesthesia. More recently, Silva et al. [3] used very short stimulus duration and reported that the CBV onset preceded the BOLD onset which appears to be inconsistent with Mandeville et al.'s data [2]. Furthermore, the precise CBF and CBV coupling and onset times remains to be determined. In this study, we further investigated the CBF, BOLD and CBV fMRI dynamics at high temporal resolution (0.5s) in a single setting and the same ROI in order to better understand the hemodynamic coupling at the early onsets. This study was performed on a rat forepaw stimulation model under 1.1-1.2% isoflurane anesthesia [4] using the pseudo-continuous arterial spin labeling technique [5] with a 500-ms temporal resolution.

**Methods** Eight male SD rats (300-375g) were anesthetized with 2% isoflurane during placement of a femoral vein catheter and needle electrodes under the forepaw skin. Isoflurane was switched to 1.1-1.2% during imaging. Rats breathed spontaneously without mechanical ventilation. Two forepaws were stimulated simultaneously in series using 6 mA, 0.3 ms pulse duration at 3 Hz, previously optimized for isoflurane anesthetic without inducing changes in MABP [4].

Multislice CBF, BOLD and CBV (MION, 14mg/kg) imaging at 4.7T was performed with a temporal resolution of 0.5s using single-shot, gradient-echo EPI acquisition. Pseudo-continuous CBF measurements [5] were made using the two-coil system with an actively decoupled brain surface coil (2.3-cm ID), data matrix=64x64, FOV=2.56x2.56cm$^2$, two 2.0-mm slices, and TE=16ms. An Ernst flip angle was used to avoid or minimize in-flow effect. Labeled and control (BOLD) images were acquired consecutively on two separate scans. MION CBV was measured following CBF and BOLD measurement using the same parameters as the control images of the CBF measurements. The forepaw stimulation consisted of 3 epochs of 60s OFF, and 20s ON.

CBF, BOLD and CBV percent changes were calculated for the primary forepaw somatosenory cortices. CBF time courses were deconvolved [5] to remove the $T_1$ saturation effect due to pseudo-continuous labeling technique. Onset times (10% above baseline) and peak times (90% of maximum) were tabulated.

**Results** Representative single-animal activation maps and the group-average (normalized) time courses of the CBF, BOLD and CBV fMRI are shown in **Fig. 1**. Robust activations were observed. The average CBF, BOLD and CBV percent changes were 30±5, 1.1±0.3, and 6.7±0.8%, respectively. The expanded time courses depicting the onset and peak times of the three fMRI signals are shown in **Fig 2**. CBV increased (slightly) first but grew slower over time. CBF started out slightly later than CBV but increased and peaked faster than CBV. BOLD showed the latest onset and peaked last. The onset times for CBF, CBV and BOLD signals were 0.68±0.51, 0.67±0.40, and 0.95±0.54 s, respectively. The peak times of the CBF, CBV and BOLD signals were 4.5±1.1, 5.0±2.3 and 5.8±2.6 s, respectively.

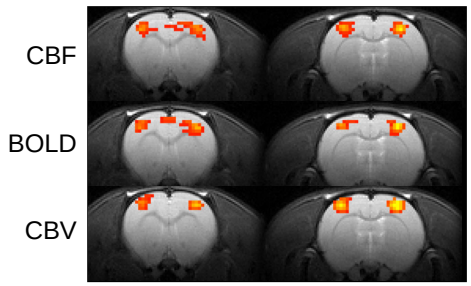
**Discussion** Our data showed that CBV preceded CBF increase slightly but CBF caught up and peaked first. Both CBF and CBV peaked before the BOLD responses. There are consents in the video laser Doppler measurement literatures (which could distinguish arterioles, capillaries and venules on the cortical surface) that the CBV in the arterioles increase first (actively dilate) which drives the subsequent and passive CBF increase. In the venules and veins, CBV increased passively as the result of upstream CBF increase. Since majority of the vasodilation occurs at the arteriole end, CBV and CBF data herein are likely to be weighted toward the arteriole side of the vasculature. In contrast, the BOLD signals are likely weighted toward the venule/venous side of the vasculature where the stimulus-evoked deoxyhemoglobin saturation changes are likely the largest. Thus, our data are in good agreement with the dynamic of different known signal sources, the classic video laser Doppler measurements, Silva's CBV and BOLD measurements [3] but appeared to be inconsistent with Mandeville's CBV and BOLD measurements. We do not have an explanation for this apparent discrepancy but it could be due to anesthetics, field strength, MR parameters, and/or the strength of stimulation.

Silva et al. reported the CBF and BOLD onset times (at 9.4T under α-chloralose anesthesia and mechanical ventilation) to be 0.6s and 1.1s [1], respectively, compared to our values of 0.7s and 0.9s. The BOLD peak time lagged CBV peak time by ~800ms [3] (at 11.7T under α-chloralose anesthesia and mechanical ventilation), compared to our value of 1.3s. Albeit differences in experimental conditions, anesthetics, field strength and stimulation duration, our results are in reasonable agreements. In particular, different field strengths could result in different sensitivity to different vessels sizes particular for the BOLD and CBV fMRI signals which could also modulate the relative onset and peak times. Further investigations of these factors are important as the precise coupling form the basis of the fMRI signals.

**Conclusion** This study reported a CBF, CBV and BOLD fMRI responses with high temporal resolution in a single setting and using the same ROI. The precise dynamic coupling of neural activity with CBF and CBV has strong implications to the BOLD signal dynamics and should reflect the $CMRO_2$ dynamics during the early phase, which is generally calculated based on BOLD and CBF (or CBV) measurements. Dynamic $CMRO_2$ changes from these data sets are currently being investigated.

**Reference** [1] Silva et al., JCBFM 2000, 20:201. [2] Mandeville MRM 1998, 39:615. [3] Silva et al., ISMRM 2004. [4] Liu et al., MRM 2004, 52:277. [5] Silva et al., MRM 2001, 42:425.

**Figure 1A**




**1B**

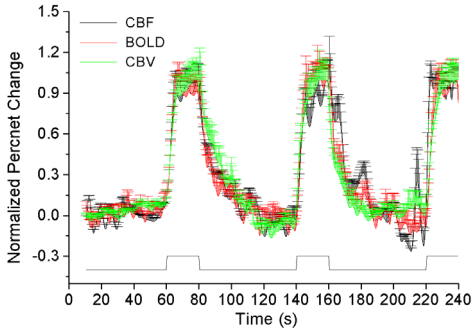



**Figure 2**