Specificity and Stability of BOLD and CBV-based Mapping Signals for High Resolution Functional Mapping at Sub-millimeter Resolution

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Introduction

Recent studies suggest that high field fMRI can map activity-associated changes in brain metabolic and hemodynamic responses with a sensitivity and resolution that allows examination of brain responses at the level of the individual modules/cortical columns that are the fundamental computational units in the brain. Both BOLD- and CBV-based functional contrast have been employed as mapping signals for these ultra-high resolution studies at high field. Several studies in visual cortex have suggested that BOLD signals may be less focal and module-specific than CBV signals (Fukuda et al., 2006, Jin et al., 2008). However studies in sensory cortex have demonstrated stable, reproducible high resolution functional maps at high field (9.4T) using both gradient echo (GE) and spin echo (SE) BOLD contrast (Zhang et al 2007, Chen et al 2007, Moon et al 2007). For longitudinal studies such as those aimed at mapping cortical plasticity, the ability to obtain sensitive and stable mapping signals is essential. However, a direct comparison of the sensitivity, stability and reproducibility of BOLD and CBV signals at sub-millimeter scale within and across imaging sessions remains lacking. Therefore, in the present study, we mapped single digit activations in primary somatosensory area 3b in a well characterized non-human primate model at 9.4T with a subtle physiological vibrotactile stimulus, and compared the spatial extents and magnitudes of BOLD (GE and SE) and CBV signal based responses within and across imaging sessions.

Methods

Three squirrel monkeys were anesthetized (isoflurane 0.5-0.8%), mechanically ventilated, and placed head was stabilized in an MR compatible head frame. Vital signs were monitored and maintained constant throughout the imaging session. MR images were acquired on 9.4T Varian magnet using a 3 cm surface transmit-receive coil positioned over the primary somatosensory cortex. T2*-weighted gradient echo structural images (TR/TE 200/16 ms, 16 slices, 512X512 matrix; 78x78x500 μm^3 resolution) were acquired to identify cortical venous structures that were used to locate SI cortex and provide structural features for coregistration of fMRI maps across imaging sessions. Seven alternating 30 s blocks of baseline and vibrotactile stimulation were delivered per imaging run. For fMRI, 2-shot, multi-slice GE- (TE/TR 16/750 ms) and SE-EPI (TE/TR 30/1500 ms) were acquired with an in-plane resolution of 273x273 μm^2. The same GE-EPI sequence, with shorter TE=10 ms was used for CBV mapping, beginning 10 minutes following a slow i.v. bolus of MION (12-16 mg/kg). All study procedures were approved by the Vanderbilt IACUC. Data were identically analyzed: individual imaging runs were pre-conditioned using standard high- and low-pass filters for drift correction and removal of high frequency noise, then runs using the same functional contrast were combined to generate functional maps thresholded at $p<10^{-5}$ (uncorrected), k=2. The amplitude and area of single digit activation in area 3b was then determined for each session, and compared for stability across sessions.

Results

Fig 1 compares representative activation maps obtained from GE- and SE-BOLD (Fig 1A) and GE-BOLD and –CBV (Fig 1B), overlaid on a high-resolution structural image that reveals the detailed vascular architecture used as coregistration landmarks. While the sites of digit activation identified by GE-, SE-BOLD and CBV signals co-localized, the area of activation (in mm^2) was significantly larger for GE-BOLD than for either SE-BOLD or CBV activations (Table 1). While the lower functional contrast of the SE-BOLD, compared with the GE-BOLD signal may partly account for its smaller area of significant signal change, this does not explain the similar more focal area of signal change observed in the CBV maps, since the mean CBV signal change was significantly greater than the GE-BOLD response (Table 1). Furthermore, the variability of both the area of signal change, and mean signal change, were significantly lower for both SE-BOLD and CBV mapping.

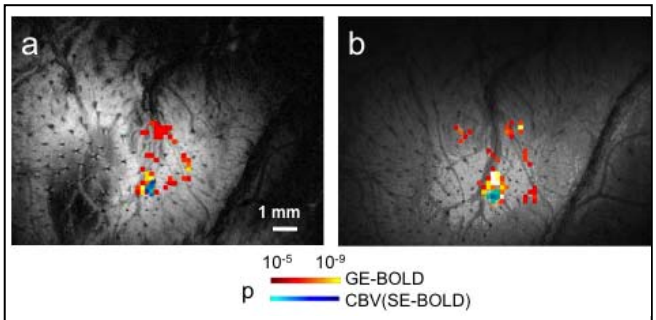

Fig. 1: Activation maps collected using (a) SE- vs GE-BOLD and (b) CBV vs GE-BOLD.

	Area of signal change (mm^2 ± s.e.m) [CV]	Mean signal change (% ± s.e.m.) [CV]
GE-BOLD (n=12)	2.07 ± 0.35 [0.56]	0.78 ± 0.07 [0.32]
SE-BOLD (n=6)	0.85 ± 0.06 [0.14]	0.56 ± 0.04 [0.14]
GE-CBV (n=6)	1.10 ± 0.11[0.22]	-1.27 ± 0.11 [0.19]

Table 1: Mean area and amplitude of significant signal change in area 3b associated with single digit stimulation.

Discussion

While all three mapping signals identify robust activations in response to single digit activation in area 3b, there were significant differences both in area of significant signal change, and in mean fractional signal change within area 3b. The smaller and co-localized area of activation observed with SE-BOLD and CBV, taken together with the significantly greater mean signal change observed with the CBV mapping signal, are consistent with previous studies suggesting that these mapping signals may provide more focal co-localization with the underlying neural response. The present data further suggest that at high field strengths, the increased functional contrast of CBV mapping will allow robust functional mapping at a resolution allowing studies of the dynamics of individual cortical modules.

References

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