CBV-based fMRI has improved temporal resolution compared to BOLD fMRI

AC Silva, AP Koretsky, P Kellman, and JH Duyn

Introduction: BOLD fMRI contrast results from several processes with different timescales. These include vascular dilation, a flow response, and the transit hemoglobin through the cerebral vasculature. Together, these processes add up to an impulse response (IR) with a 3-6 s full width at half maximum amplitude (FWHM) in humans. The purpose of this work was to investigate 1) if the reduced vascular transit times in rat result in improved temporal resolution, and 2) to what extent is the resolution limited by hemoglobin transit.

Materials and Methods: Experiments were performed on adult male Sprague-Dawley rats (n=7) under α-chloralose anesthesia [1] on an 11.7 T/31cm Bruker scanner. BOLD (n=7) and CBV (n=5, subset) fMRI was performed using a gradient-recalled echo (GRE) EPI sequence with the following parameters: resolution 300x300x1000μm^3, TE = 16-20 ms (BOLD) or 9.1-20 ms (CBV), TR = 500ms or 1000ms. To allow estimation of the fMRI IR width, bilateral electrical forepaw stimulation (333 μs pulses, 2 mA amplitude) was performed using an M-sequence paradigm with a 500ms or 1000ms baseperiod and 255 bin length, and inverse repeat [2]. Two runs were performed each for BOLD and CBV fMRI. For CBV fMRI, a dose of 20 mg/kg of iron oxide was injected intravenously 5 minutes before commencing the CBV studies. The IR was calculated from correlation analysis [2]. In activated pixels, FWHM and time-to-peak of the IR were estimated after 5-10 fold temporal interpolation.

Results and Discussion: All BOLD and 3 of the CBV fMRI studies showed substantial activation (2 CBV studies were technical failures). An example is given in the figures. Regions of activation were significantly larger in BOLD (Fig. 1, left column), than in CBV (Fig. 1, right column), attributed to BOLD effects in large draining veins. A substantial spread in BOLD FWHM (Fig. 1, middle row) and TTP (Fig. 1, bottom row) over the activated area was observed, with the responses showing a longer delay in large pial veins. This effect was much reduced in the CBV data, presumed to have less contamination from larger veins [3].
In all rats, the CBV IR was narrower and peaked earlier than the BOLD IR (Figs. 1,2). Interestingly, the CBV IR did not return to baseline for many seconds (Fig. 2), consistent with other CBV-based fMRI studies in rats [4]. Averaged BOLD fMRI FWHM and TTP were 2.3±0.6s and 2.7±0.6s (n=8), respectively. These values are significantly reduced compared to human values, suggesting a substantial contribution of flow response and hemoglobin transit to the human IR. Furthermore, CBV FWHM (1.6±0.2s,n=3) and TTP (1.9±0.3s,n=3) were even shorter than their BOLD counterparts, suggesting a substantial hemoglobin transit effect to the BOLD IR in rats. We conclude that CBV fMRI allows for improved temporal resolution, and that the temporal resolution of neurovascular control mechanisms is below 1.6s FWHM.

References: [1] Silva, PNAS 20020; [2] Kellman, Neuroimage 2003; [3] Mandeville, MRM 1999; [4] Mandeville, JCBF 1999.