Evaluation of Diffusion fMRI (DfMRI) with Short Event Related Paradigms

T. Aso[1], C. Poupon[1], S-I. Urayama[2], H. Fukuyama[2], and D. Le Bihan[1,2]

[1]NeuroSpin, I2BM/DSV/CEA, Gif-sur-yvette, France, [2]Human Brain Research Center, Kyoto University Graduate School of Medicine, Kyoto, Japan

INTRODUCTION: Visual activation can be detected with heavily sensitized diffusion-fMRI (DfMRI) [1,2]. The striking temporal precedence of the diffusion response to BOLD suggests a non-vascular source. However, a residual tissue T2' component sensitive to vascular (BOLD) effects also remains present in the DfMRI signal [2,3]. The purpose of this present study was to build a response function optimized for DfMRI taking into account both diffusion and vascular dynamics, and to evaluate it with an ultra-short event-related stimulation mode.

BACKGROUND: Assuming linearity of the neural response the observed DfMRI (spin-echo) signal results from the convolution of the activation paradigm with an intrinsic response function which characterizes the underlying elementary processes. While the Hemodynamic Response Function (HRF) represents the $T2'_t$ intrinsic response following a Dirac impulse stimulation, we have introduced a Diffusion Response Function (DRF) which represents the intrinsic pure diffusion response [2]. As the diffusion and hemodynamic (BOLD) responses likely have a different physiological origin the HRF (red in Fig.1 inset) and DRF (blue in Fig.1 inset) are expected to be different in shape and time, and additive. The observed DfMRI signal response can then be written as:

$$dS_{obs}/S_{obs}(t) = [(1-\beta)DRF + \beta HRF] \otimes P(t) \equiv [DhRF] \otimes P(t)$$

where P(t) is the paradigm time course and β is the fractional contribution of the residual T2'-BOLD component to the overall diffusion-sensitized signal. β is expected to vary with TE and the b values, as well as among voxels [3]. Here the DhRF represents the overall DfMRI impulsional response with its diffusion and T2' components. An iterative fitting procedure was used to determine the DRF and estimate β from DfMRI data obtained with b=1800s/mm^2 in the anatomically defined visual cortex of 17 subjects using 10.5s and 21s visual stimuli [2]. β was found to be 26% (peak amplitude) (Fig.1). In the figure inset the color-encoding in the DhRF (bold curve) highlights the temporal evolution of the DRF/HRF dominance [3]. In the early phase of the DhRF response the diffusion component predominates, while the HRF takes over at the end of the stimulation. The HRF was estimated from (T2*) BOLD data acquired with a TE=30ms gradient-echo (GE) sequence, although DfMRI data were obtained with a TE=83ms, b=0 spin-echo (T2') sequence. However, no difference could be found between the GE BOLD and the b=0 SE signal time courses (Fig. 2).

Figure 1

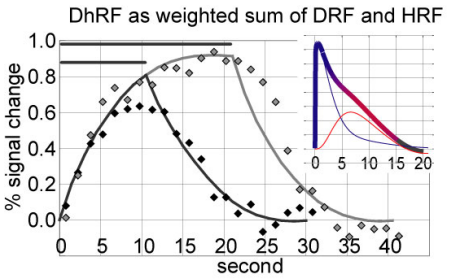


Figure 2

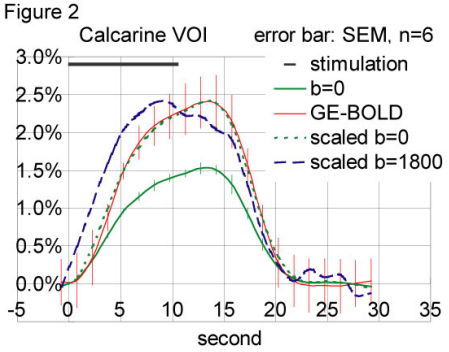


Figure 3 Short-ISI (4.5s) responses in V1

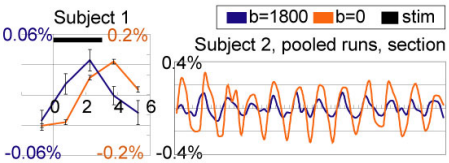
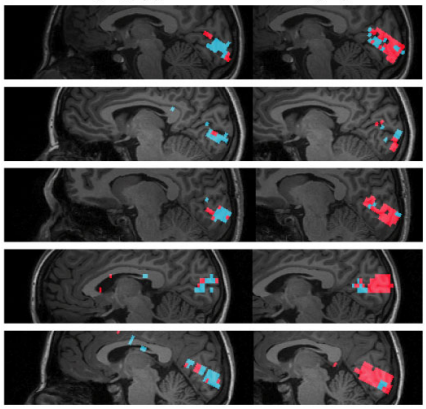


Figure 4



MATERIALS & METHODS: We studied 14 healthy subjects including 6 for preliminary T2'/T2* comparison in Figure 2. MR images were acquired using a 3T scanner with a 32-channel head coil. 7.5Hz flickering dartboard was projected via an LCD projector. The visual stimulation lasted 10.5s in the preliminary test and 3s in the following experiments. A very short, constant ISI of 4.5s was tested on 3 subjects and 5 subjects underwent Event-Related (ER)-DfMRI with random ISIs ranging 0-24s (mean 14.6s). Head was strictly constrained by foam pads and instruction was given to prevent head motion.

Data acquisition: We used a twice refocused, SE EPI sequence sensitized to diffusion by an interleaved pair of bipolar gradient pulses (b=1800s/mm², along X, Y and Z axes). The basic acquisition parameters were: 64 × 64 pixels, 192mm FOV, 3.5-mm slice thickness with 20% gap, TR = 1500 ms, TE = 76 ms, 7 slices. For 2 subjects in ER-DfMRI, another setting was tested expecting the same result: 96 × 96 pixels, 240mm FOV, 3.8-mm slice thickness, 5 slices and TE = 83 ms. Each run lasted 200s. Between the DfMRI runs, b=0 SE-EPI images were also acquired for comparison (T2'-BOLD response).

Data processing: Slice-timing and motion correction was done using SPM5. For the short ISI, signals were extracted from anatomically-defined volume of interest (VOI) covering the calcarine sulci. For the ER-DfMRI and ER-SE BOLD data standard SPM analysis was performed but using both the canonical HRF (threshold at corrected .05) and the DhRF (threshold at uncorrected .001) as the basis function following 6x6 in-plane spatial smoothing.

RESULTS AND DISCUSSION: The DfMRI (b=1800) response to periodic stimulation with 4.5s ISI clearly showed an earlier response than with SE(T2')-BOLD for 3 subjects (Fig. 3), confirming earlier reports with longer stimuli and ISIs (1,2). The ER-DfMRI signal changes were better predicted by using the DhRF than the canonical HRF by comparing the goodness of fit (t values) for each voxel, while the HRF was better suited for the SE-BOLD data (Fig. 4, color-encoding according to the larger t-value: blue for DhRF, red for HRF). The linearity assumption seems to hold to some extent with ultra-short ER DfMRI paradigms. Interestingly the diffusion responses to 4.5s ISI occurred not only earlier but were more uniform across subjects while there was significant variation in the SE-BOLD response across subjects. The observed BOLD responses to short ISI were also not well predicted by canonical HRF, suggesting nonlinearity in neurovascular coupling [4, 5]. Although further investigation is necessary, the diffusion response appears more stable than BOLD.

REFERENCES 1. Le Bihan et al., PNAS 103 (2006); 2. Aso et al , abs#2387 ISMRM 2008; 3. Le Bihan et al., submitted ISMRM 2009; 4. Handwerker et al, NeuroImage 21 (2003); 5. Tuan et al. International Journal of Imaging Systems and Technology 18 (2008).