Investigating the field strength dependence of BOLD onset time

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Audience: Those interested in fMRI physiology and temporal characteristics of BOLD. **Purpose:** The gradient echo BOLD signal onset has been shown to be earlier at higher field[1]. Assuming this relates to a delay in the changes in venous oxygenation (Yv) and volume (CBVv) compared to the changes in the capillaries and arteries[2] then possible explanations are: **(a)** increased arterial contributions to the BOLD signal at high field due to a relative increase in the ratio of arterial to venous T_2* **(b)** increased extravascular (EV) effects from capillaries at high field due to the increased frequency shift[3] **(c)** inflow of fresh blood into the imaging slice causing an early signal increase which has a greater effect at high field due to increased blood T_1. **Aim:** To test these competing hypotheses using fMRI data previously acquired at 1.5, 3 and 7 T[4] and BOLD signal models.

Methods: Six healthy volunteers were scanned on 1.5, 3 and 7 T Philips Achieva systems with an 8-ch SENSE receive coil (1.5/3 T), or 16-ch SENSE receive coil (7T). Axial EPI images with a reduced FOV (128x192 mm) were acquired over the occipital lobe (TR=1 s, TE = 55/45/32 ms, 2 mm isotropic voxels with 8/10/10 slices and no slice gap, SENSE =2/2/3; 1.5T/3T/7T respectively). The visual task (8Hz red LED goggles) comprised of 60s initial baseline, followed by 5s ON and 55s OFF repeated for 4 minutes at 1.5T, 6 minutes at 3T & 7T. These scan sessions were repeated for 3 (1.5T) and 2 (3/7T) runs both with flow suppression (FS; b=100smm^{-2}) and without flow suppression (NoFS). Whole head EPI and MPRAGE data were acquired at each field for cross-field registration. *Analysis:* Datasets were motion corrected, high-pass temporal filtered and spatially smoothed. To investigate the spatial distribution of BOLD transients, a serial t-test was performed on the average trial providing a t-statistic map for each timepoint across the trial. Standard activation maps were formed based on the whole timecourse ($Z>2.3$;$P_{corr}<0.05$;gamma variate hrf) using FEAT (FSL, Oxford). A common ROI was formed from the intersection of NoFS activation maps across all three field strengths (co-registered using FLIRT (FSL)). *Modelling:* BOLD signal was modelled as the sum of the signal contributions from 4 compartments[5,6] (3 intravascular (IV) compartments of arteries (*a*), veins (*v*), and capillaries containing deoxygenated blood (*c*), and an EV compartment; fig 2a), each compartment weighted according to varying T_2* and T_1 values for each field strength[7,8]. Arterial volume was modelled directly from cerebral blood flow (CBF) using Grubb constant = $^1/_{1.2}$[9]. CBV_v was modelled assuming delayed compliance[6], and Y*v* change was modelled with a delay of 2 s with respect to the CBF change. Capillaries were modelled as not dilating and capillary oxygenation (Y*c*) change was not delayed. To test hypothesis (a) the BOLD signal due to each compartment including its EV effect was simulated for varying arterial blood volumes. To test hypothesis (b) capillary and small venule contributions to EV BOLD signal were weighted differently across fields, by extrapolation from Monte Carlo simulations[3]; this takes account of the interacting effects of frequency-shift and vessel radius on EV signal, resulting in smaller EV capillary contributions at low field.

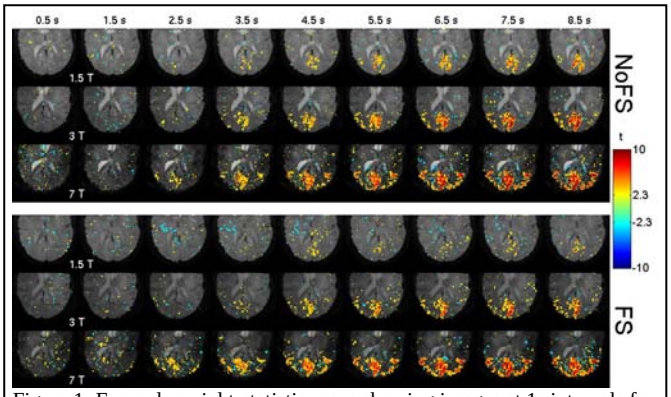

Figure 1: Example serial t-statistic maps showing images at 1s intervals for the first 9 s following visual stimulus onset.

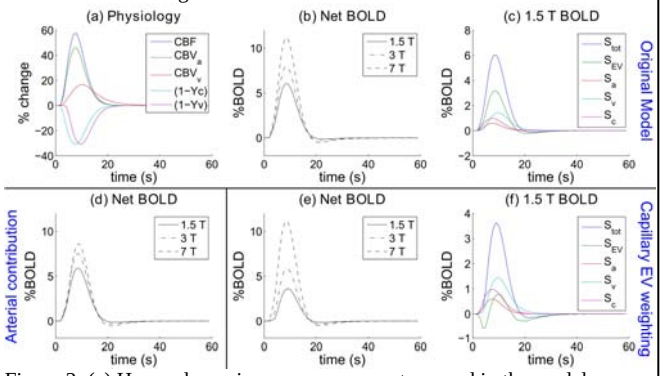

Figure 2: (a) Haemodynamic response parameters used in the model. (b,d,e) show the net BOLD signal across field, (c,f) show the component signal contributions (S) at 1.5T. (b,c) Signals modelled assuming no attenuation of EV capillary signal and $CBV_{a,0}$=1%. (d) the effect of increasing $CBV_{a,0}$ to 5% . (e+f) the effect of different weightings of capillary and venous EV signals ($CBV_{a,0}$ =1%).

Results: Fig. 1 shows the earlier onset of the BOLD response at 7T in the serial t-statistic maps. Within the common ROI, BOLD onset time reduced with increasing field strength (P=0.0009, 2-way ANOVA) from 2.9±0.1/3.3±0.2s at 1.5T, to 1.9±0.2/2.0±0.3s at 7T (NoFS/FS, mean±SEM over subjects). *Hypothesis (a):* Fig. 2 b,c&d show that even by increasing the arterial blood volume fraction ($CBV_{a,0}$), arterial contributions cannot explain the shift in onset time for the 4 compartment BOLD signal model. *Hypothesis (b):* Fig. 2 b&c show the signals that are obtained if it is assumed that the EV capillary signal does not change with field strength, but Fig. 2e&f show the same result with the EV capillary signal attenuated with field strength according to[3]. *Hypothesis (c):* Applying FS to reduce inflow effects did not remove the tendency for an earlier onset time at higher field.

Discussion: These results rule out the possibility that inflow effects or different arterial signal weightings are responsible for the earlier onset time at high field. However they do show that different relative capillary signal contributions at high field[3], combined with flow dispersion delaying venous oxygenation changes[2], could cause this field-dependent onset time shift. This work used results from previous Monte Carlo simulations[3], but additional simulations are required to fully explore the effect of different capillary contributions at each field strength and TE. The modest flow suppression used here reduced the effects of inflow and intravascular signal (which are different across field strengths) but did not reduce the delay with field, further supporting an EV mechanism. The experiments used here had a TR of 1s (to preserve SNR at 1.5T), but cross field data acquired at shorter TR could be used to measure the venular transit time and flow dispersion. The frequency shift could also be perturbed using an IV contrast agent at a single magnetic field, removing the need to make measurements across field strengths.

Conclusion: The decrease in onset time observed with increasing field strength is likely to be due to attenuated EV capillary component at 1.5T combined with the delayed change in venous blood oxygenation.

References 1. van der Zwaag et al. NeuroImage 47:1425-1434 (2009); 2. de Zwart et al. NeuroImage 24:667-677 (2005); 3. Boxerman et al. MRM 34:555-566 (1995); 4. Driver et al. Proc. ISMRM 18: 3478 (2010); 5. Griffeth and Buxton NeuroImage 58:198-212 (2011); 6. Kong et al. JCBFM 24:1382-1392 (2004); 7. Uludag et al. NeuroImage 48:150-165 (2009); 8. Blockley et al. MRM 60:1313-1320 (2008); 9. Lee et al. MRM 45:791-800 (2001). **Funded by the UK MRC**