Changes in CBVa and CBF haemodynamic response with stimulus duration of 4.8 and 9.6 s.

R. Wesolowski[1], R. Coxon[1], A. G. Gardener[1], S. T. Francis[1], and P. A. Gowland[1]

[1]Sir Peter Mansfield Magnetic Resonance Centre, University of Nottingham, Nottingham, United Kingdom

Introduction: Arterial CBV (CBVa) and CBF are important haemodynamic inputs to any model of the BOLD effect[1-3]. Measurement of activation-induced change in arterial CBV (CBVa) and CBF is possible using standard arterial spin labeling (ASL) techniques by performing two ASL experiments across a range of TI's both with and without diffusion weighting[4]. However, such an acquisition is time consuming, particularly if CBVa measures are required both at rest and on activation. Recently, we have shown that Look-Locher Echo Planar Imaging (LL-EPI)[5] can be combined with the FAIR ASL technique to quantify either CBVa[6] or CBF[7] with high sensitivity, depending on the pulse timings used. The aim of this work is to use these LL-FAIR sequences to measure the time course of changes in both these parameters with high temporal resolution (2.4 s) and high SNR, for short (4.8 s) and long (9.6 s) stimuli. The LL-EPI pulse sequence comprises a single hyperbolic secant inversion pulse followed by a series of EPI readout modules each with an RF pulse of flip angle α, and separated by a time TA (Figure 1). The combination of the LL-EPI sequence with FAIR (LL-FAIR) provides flow sensitivity by alternating the width of the inversion slice between being selective and non-selective. The LL-EPI readout pulses repeatedly sample labeled blood magnetization as it flows through the imaging slice. We have previously shown that if the LL-EPI sampling uses low flip angle pulses applied at time interval TA greater than the tissue transit time, then this sequence is sensitive to CBF, whereas if high flip angle pulses are applied more rapidly then the blood is suppressed before it exchanges with the tissue, and so the sequence is sensitive solely to CBVa.

Methods: The LL-FAIR sequence was implemented on a Philips 3T Achieva scanner using a SENSE head gradient coil. The timings used have previously been optimized for the measurement of CBF[7] and CBVa[6] at 3T (CBF: TI = 600 ms, TA = 360 ms, α = 40°, 5 readout pulses; CBVa: TI = 150 ms, TA = 100 ms, α = 50°, 21 readout pulses). The TR between inversion pulses was 2.4 s (4.8 s per label/non-label pair). The imaging slice was 5 mm thick and the inversion pulse alternated between 30 and 200 mm thick for the selective and non-selective conditions. The EPI echo time was 16 ms and the image resolution was 3x3x5 mm^3. The flip angle of the final LL-EPI readout pulse for both the CBVa and CBF sequences was 90°, to maximize SNR and to provide suppression of the imaging slice to reduce any offset signals due to imperfections between selective and non-selective pulses. An additional pre-saturation pulse was applied to the imaging slices immediately after the inversion pulse to further suppress the effect of any pulse imperfections, and to simplify fitting.

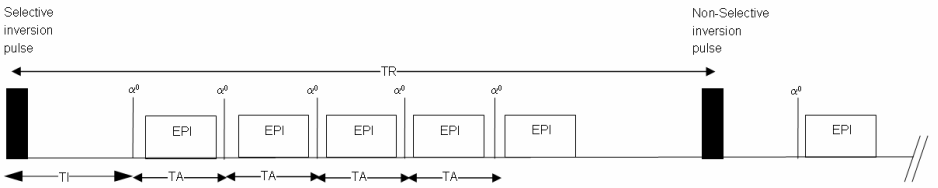

Figure 1. LL–FAIR sequence.

Four healthy volunteers gave informed consent and participated in visual activation experiments on two separate days. The visual stimulus was an 8 Hz bright red LED light which was shone at the eyes down light pipes for 4.8 s separated by 26.4 s of rest and repeated 31 times (first experiment) or 9.6 s separated by 50.4 s of rest and repeated 16 times (second experiment). Initially 3 LL-EPI sets were acquired in order to allow for T_1 saturation effects. An odd number of LL-FAIR acquisitions were made per stimulus cycle, resulting in the experiment being jittered to give an achievable effective temporal resolution of 2.4 s.

Analysis: Although this data can be fitted for CBF, in this experiment we performed a qualitative analysis by simply co-adding the signal from the different readout pulses following each inversion pulse (all images for CBF, and four images where the greatest signal change for CBVa was observed in the unaveraged difference images). This to provide a high SNR CBF and CBVa weighted data set. Difference images (from the subtraction of consecutive selective and non-selective pairs) were calculated to give a time series of CBF and CBVa weighted images. The CBF response to the stimulus could clearly be seen on these images, even before averaging the trials together. Regions of interest were drawn around the area showing a CBF response on the raw image, a grey matter mask (obtained from the first LL-EPI image acquired after the inversion pulse which was relatively T_1 weighted) was then applied to these ROIs. The signal in the grey matter pixels within the activated region was averaged for each image, and then the data was average across trials to provide a time course of the CBF and CBVa response to the visual stimuli.

Results: Figure 2 shows the CBF weighted images for a single trial of the stimulus (i.e. no averaging of images has been carried out). This single trial CBF data illustrates the considerable gains in signal to noise than can be achieved by using LL-FAIR compared to FAIR. Figure 3(A) shows the CBVa responses averaged over all cycles and all four subjects for the short and long visual stimuli. Figure 3(B) shows the corresponding CBF responses. In this case we averaged all the data sets together, but we found that in general adequate SNR could be obtained with averages of only 10 data sets.

Figure 2. Single cycle images acquired over 31.2 s, showing resting perfusion and response to activation in V1 on images 3-7.

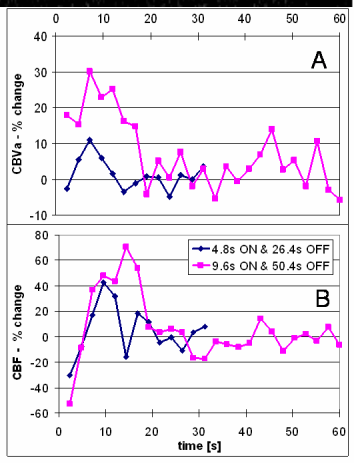

Figure 3. (A) % CBVa signal change and (B) % CBF signal change averaged across subjects for short (4.8s) and long (9.6s) stimuli.

Discussion: We have extended previous work that has measured the change in the CBF haemodynamic response to various lengths of visual stimuli[3] to also measure the change in the CBVa haemodynamic response. The CBF changes observed are consistent with those in the literature[3] and show a similar degree of variability for these short stimuli. CBVa changes precede CBF changes. This data will provide important input parameters for models of the BOLD effect. In future we will investigate the optimum methods of combining the data from the different readout pulses, taking account of changes in transit time. We will also fit the data to models previously described to obtain quantitative CBVa and CBF response curves[6,7]. Since we have adequate SNR to measure response to activation in relatively short experiments, future work will also study the effects of intrasubject variability during a trial, intrasubject variability between trials and intersubject variability.

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References: 1) Buxton *et al.*, Magn. Reson. Med., 39:855-864 (1998). 2)Behzadi *et al.*, NeuroImage, 25:1100-1111 (2005). 3) Miller *et al.*, Hum. Brain. Mapp., 12:1-12 (2001). 4) Barbier *et al.*, Magn.Reson.Med.,45;1021-1029 (2001). 5) Look & Locher, Rev. Sci. Inst, 41, 250-1 (1970). 6) Brookes *et al.*, MRM under review. 7) Francis *et al.*, MRM submitted.