Investigating the feasibility of correlating evoked responses and BOLD signals using simultaneous EEG/fMRI at 7T.

K. J. Mullinger[1], C. M. Stevenson[1], S. T. Francis[1], and R. W. Bowtell[1]
[1]Sir Peter Mansfield Magnetic Resonance Center, School of Physics and Astronomy, University of Nottingham, Nottingham, Nottinghamshire, United Kingdom

Introduction: Haemodynamic and electrical responses may show unpredictable variations in magnitude over repeated trials due to habituation or modulation of attention. Correlations of the different responses can be assessed by simultaneously monitoring EEG and fMRI signals, with single trial estimates of the BOLD and evoked responses potentially offering the best measure [1]. The increased contrast-to-noise ratio of BOLD signals at 7T allows better characterisation of haemodynamic responses, but operation at high magnetic field produces greater noise in EEG recordings made during simultaneous fMRI acquisition [2]. Here we investigate the minimum number of trials needed to characterise the evoked response to a somatosensory stimulus at 7T, and investigate whether correlations between BOLD and evoked responses can be observed.

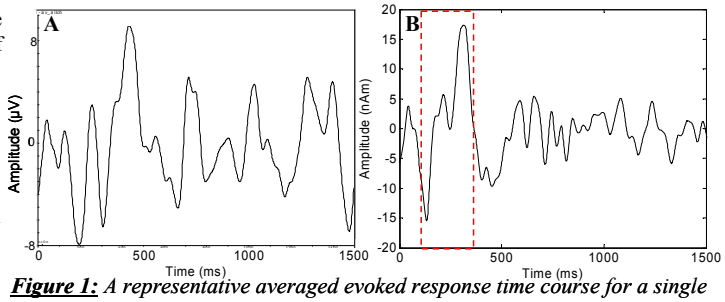

Figure 1: *A representative averaged evoked response time course for a single subject from electrode C3 (A) and the virtual electrode in S1 (B). Red box denotes time window considered for maximum and minimum peaks.*

Methods: fMRI and EEG data were acquired simultaneously using a Philips Achieva 7T MR scanner and a 64-channel EEG system (Brain Products, Munich). Padding was used to position the EEG leads away from the head so as to prevent MR signal loss due to RF inhomogeneity. A standard EPI sequence was implemented (2×2×3 mm^3 voxels; TR/TE =2000/25ms). Cardiac pulse and respiration were monitored using the scanner's physiological logging system. The scanner and EEG clocks were synchronised [3]. Electrode positions on the scalp were digitized using a Polhemus (Isotrack) system. Data were acquired on nine, right-handed female subjects. Vibrotactile stimuli with ~1mm amplitude and 33 Hz frequency (flutter) were applied to an area of ~ 4 mm^2 on the tip of the right index finger using piezoelectric stimulators. Data were recorded over 40 trials (10s on and 20s off), along with (4-5) blank trials, which subjects were asked to count so as to maintain attention to the task.

Analysis: *EEG:* Gradient and pulse artefact correction via average artefact subtraction was implemented in Brain Vision Analyzer2 [4-5]. Noisy trials and/or channels were discounted by inspection of the data and two subjects were excluded from further analysis due to the presence of a large number of rejected trials, presumably resulting from interference due to movement in the strong magnetic field. Another subject was removed from analysis as they did not attend (incorrect count of blank trials). Following artefact correction, data were down-sampled to 600Hz and re-referenced to an average of all non-noisy channels so as to limit the effect of residual pulse artefact. Data were filtered 1-20Hz and a notch filter applied at 33Hz to reduce interference from the stimulus. Time courses of electrical activity (Virtual Electrode (VE) traces) in anatomically identified, left primary somatosensory cortex (S1) were generated for each subject using weights derived from a regularised, scalar beamformer [6]. Trials were averaged to ascertain the time window containing the individual's evoked response. The maximum and minimum amplitude within this time window was ascertained for averages of different numbers of trials. Baseline noise and noise variance was estimated from the standard deviation of the signal in the penultimate second of the averaged data. The signal-to-noise ratio (SNR) of the evoked response was calculated for the different averages and converted to a P-value. Successful detection of an evoked response ($P \leq 0.01$) required data to be averaged across at least 10 trials. A peak-to-peak measure of the evoked response was therefore calculated from the averages of 10 successive trials across the whole experiment and the associated relative error and variance calculated.

fMRI: Data analysis was carried out using SPM5, after application of RETROICOR to reduce physiological noise. Significant activity (P<0.05 corrected) in the SPM was used to identify a ROI in left S1. An average timecourse was extracted from the ROI and the amplitude of the BOLD response in each trial and in the averages of 10 successive trials were found. The amplitude of the BOLD response was calculated as the relative difference of the average signals at the maximum ± 2 s of the haemodynamic response and at baseline (last 6s of each cycle).

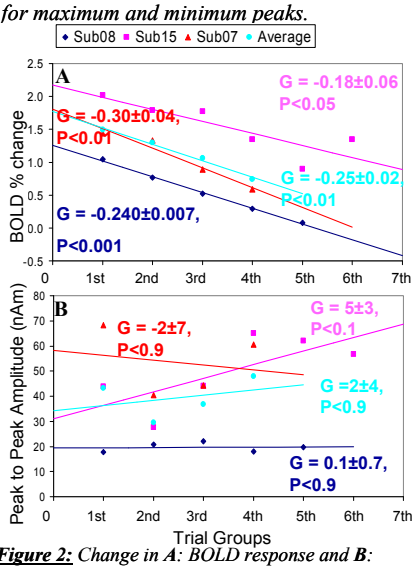

Figure 2: *Change in **A**: BOLD response and **B**: evoked response with trials for individual subjects and group average. Trials groups are 1st=1-10, 2nd=6-15, etc. Gradients and significance of linear regression are detailed for each subject.*

Results and Discussion: Figure 1 shows the averaged evoked response from a single channel (A) and the VE (B) for a subject who met the criteria that the evoked response could be detected at P≤0.01 in an average of 10 trials. For this subject an increase of 67% in the SNR of the positive peak was achieved using a VE rather than a single channel, in agreement with the previous finding that the beamformer attenuates residual artefacts [6]. Of the 6 remaining subjects, 4 showed significant (P≤0.01) positive and negative peaks in the evoked response in an average of 10 trials. fMRI data analysis was carried out on these four subjects, but one subject had to be discounted due to the poor quality of the BOLD statistical map which made it impossible to define an ROI . The remaining 3 subjects showed a significant attenuation of the BOLD response through the course of the experiment (Fig. 2A), suggesting habituation in agreement with previous findings [7-8]. This effect was not observed in the evoked electrical responses, with no subject showing a significant attenuation of peak-to-peak amplitude across trials (Fig. 2B). Correlation of the BOLD and EEG responses across trials was variable (correlation coefficients: 0.0146, -0.0895 & -0.759 for subjects 07, 08 & 15 respectively) showing no clear effect across subjects. Further analysis of the data showed that the variances of peak and baseline levels were similar for all subjects, even when multiple trials were averaged (Fig. 3). To assess whether this finding is a consequence of high noise levels in EEG data recorded at 7T, the experiment was repeated on a single subject outside the scanner. The results showed a 26% increase in the SNR of the evoked response and a reduction in the variance of the positive peak amplitude of 106% for an average over 10 trials, but despite this there was no measurable attenuation of the evoked response over 40 trials.

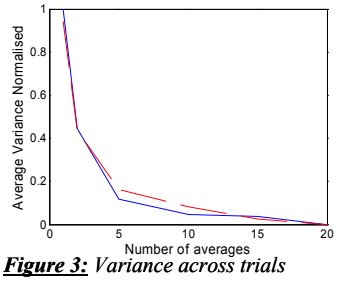

Figure 3: *Variance across trials (normalised for single trial variance of peak) in positive evoked response (blue line) and baseline (red dashed line) with number of trials averaged.*

Conclusions: Haemodynamic and evoked responses have been measured simultaneously in EEG-fMRI experiments at 7T, ensuring identical attention and habituation effects were monitored by both modalities. Between trial variance was assessed to identify the number of trials needed to observe the evoked response reliably. With this criterion attenuation of the BOLD response was seen, suggesting habituation, but no corresponding effect was observed in the evoked response. Baseline variance was found to equal that of the evoked response, thus a) there may have been no attenuation of the evoked response if baseline variance is dominated by on-going neuronal activity or b) attenuation was masked by physiological and instrumental noise sources. This analysis highlights the need to assess noise variance to interpret whether meaningful correlations between BOLD and the evoked responses are present.

References [1] Debener *et al* Trends in Cogn. Sci. **10**(12);2006 **[2]** Mullinger *et al* MRI **26**(7), 2008 **[3]** Mandelkow *et al.* NeuroImage, **32**(3): 2006 **[4]** Allen *et al* NeuroImage **8**(3):1998 **[5]** Allen *et al* NeuroImage **12**(2):2000 **[6]** Brookes *et al* NeuroImage **45**(2): 440-452 **[7]** Wright *et al* Proc ISMRM 2008 #2423 **[8]** Trulsson *et al* NeuroImage **13**(4): 2001