Exploring the relationship between natural fluctuations in electrical measures of brain activity and the BOLD response, during visual stimulation.

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Introduction

Whilst simultaneous EEG-fMRI has been used to explore correlations between alpha and beta power and resting state BOLD responses [1-3]; no work to our knowledge has been conducted to investigate whether there is a correlation between natural fluctuations in alpha power and the magnitude of the BOLD response to a conventional stimulus. A similar question relating to any correlation between natural fluctuations in the strength of the stimulus-driven electrical and BOLD responses also obtains. This study aims to address these questions via analysis of EEG and fMRI data, which were simultaneously acquired during visual stimulation.

Methods

fMRI and EEG data were acquired simultaneously using a Philips Achieva 3.0 T MR scanner and a BrainAmp MR-plus EEG amplifier, Brain Vision Recorder software (Brain Products, Munich) and the BrainCap MR electrode cap with 32 electrodes (5 kHz sampling rate). A standard EPI sequence was implemented (64×64×20 matrix, 3.25×3.25×3.00 mm^3 voxels) with TR/TE =2.2s/40ms and 20 slices were acquired Cardiac cycle timing was simultaneously recorded using the scanner's physiological monitoring system vector cardiogram (VCG) [4]. Synchronisation of the scanner and EEG clocks [5-6] was employed. A Polhemus (Isotrack) system was subsequently used to determine the electrode positions on the scalp. Subjects were screened to ensure that they exhibited easily recordable alpha power. Visual stimuli flashing at 8 Hz were presented using red LED goggles. In each of the 40 trials the stimulus was presented for 5s followed by a 30s off period. 660 EPI volumes were acquired. Presentation of the stimuli relative to fMRI acquisition was jittered across cycles to ensure maximum sampling of the BOLD response.

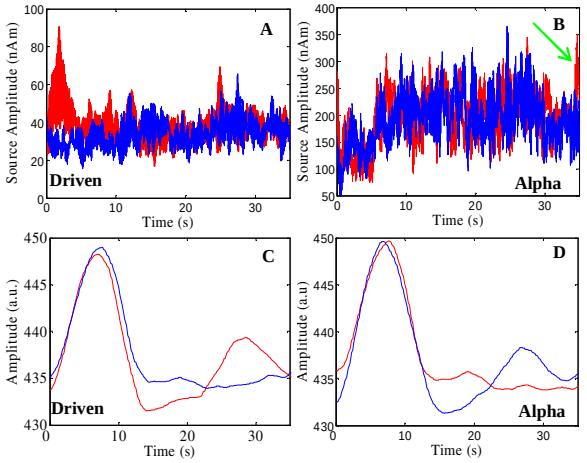

Figure 1: *The driven (**A**) & alpha power (**B**) in the top (**red**) & bottom (**blue**) quartiles when binned according to the driven power and preceding 0.25s alpha power (marked with arrow) respectively. The associated haemodynamic responses are shown in **C&D**. 0s=stimulus onset.*

Analysis

EEG: Average artefact subtraction was applied as implemented in Brain Vision Analyzer [7]. Gradient artefact correction employed an artefact template formed from the average over all *TR*-periods. Pulse artefact correction was based on R-peak markers derived from the VCG trace [6]. After artefact correction data were down-sampled to 600 Hz sampling rate.

fMRI: Image processing (realignment, and spatial smoothing with a 3 mm FWHM Gaussian kernel) was carried out using SPM5. fMRI models were set up for all trials within a study with correction for global effects via standard filtering. The results of this analysis thresholded at $p<0.001$ (corrected) were used to identify regions of interest (ROI) in the visual cortex.

After the initial analysis_a beamformer [8] was applied to 8-12Hz filtered data to create a T-stat image ($0<t_{act}<4.5s$, $5<t_{pass}<9.5s$) depicting focal areas showing a significant change in alpha power during stimulus presentation. The alpha power preceding each stimulus onset was obtained using beamformer weights ($Q^2=Tr|\mathbf{W}^T\mathbf{C}\mathbf{W}|$). Trials were sorted and binned (into quartiles) according to the measured value of the alpha power in a 0.25 or 2s time window preceding stimulus onset. The same process was carried out for the frequency band 15.5-16.5Hz to study the driven response and trials were re-binned according to the driven power measured in the first 4.5 s following stimulus onset. The haemodynamic response in the ROI was averaged over the trials in each bin for each subject, allowing evaluation of the difference in BOLD response between trials with high and low preceding alpha power and high and low driven responses. The BOLD response was taken to be the % difference between the average signal at the HRF maximum±1.5s and at baseline (last 5s of data).

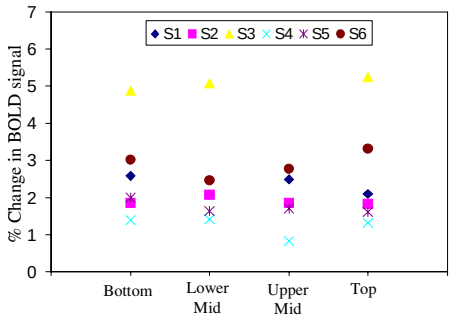

Figure 2: *The % change in BOLD signal ((max-min)/max in hrf) for each subject when the BOLD responses are binned according to alpha power in 0.25s preceding stimulus onset.*

Results and Discussion

One subject was removed from the analysis due to excessive movement during the study. The variation in preceding alpha power over the 40 trials was found to be significant varying by a factor of approximately 4 between upper and lower quartiles. The strength of the driven response varied by a factor of approximately 2. Figure 1 shows example EEG and BOLD responses averaged over trials falling in the upper and lower quartiles after ordering according to the strength of the preceding alpha power or driven response. These plots show that the BOLD and EEG responses are well characterised by averaging over 10 trials. Despite this, no consistent correlation was found between the preceding alpha power and the BOLD response when binned into quartiles according to either 2s or 0.25s of EEG data for each subject (Fig. 2). Similarly, no direct correlation between driven power and BOLD response in each quartile was found. A related finding of no correlation of alpha power and haemodynamic responses in optical and EEG measurements has previously been reported [9].

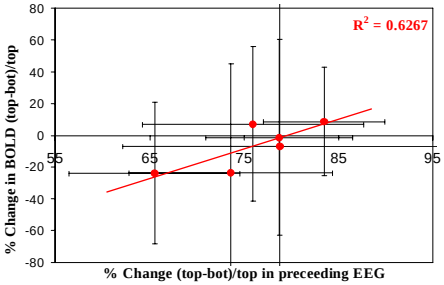

Figure 3: *Average fractional difference of the BOLD response between the upper and lower quartiles binned according to the preceding 0.25s of alpha power, plotted against the similar fractional difference in preceding alpha power for each subject.*

A correlation was found when comparing the fractional difference in the alpha power in the 0.25 s preceding stimulus onset between upper and lower quartiles (binned according to this preceding alpha power) with the corresponding fractional difference in BOLD response across subjects (Fig 3). This trend was not seen in the data binned according to the alpha power in the preceding 2s. A similar plot of the fractional difference in driven response power between upper and lower quartiles of data binned according to the strength of the driven response and the fractional difference in BOLD responses across subjects showed a similar positive trend with $R^2=0.71$. The results of this study suggest that although the preceding alpha power or driven electrical response does not directly predict the magnitude of the BOLD response in our single subject measurements, there is some evidence for correlation between the range of variation of the BOLD response and the range of variation of the EEG measures across subjects. Study of more subjects is needed to confirm the significance of the latter finding. This study further indicates the complexity of the relationship between EEG measures of electrical activity and the BOLD response

References [1] Gonclaves *et al.* NeuroImage **30**(1): 2006 **[2]** Laufs *et al.* PNAS **100**(19): 2003 **[3]** Moosman *et al.* NeuroImage **20**(1): 2003 **[4]** Chia *et al.* JMRI, **12**: 2000. **[5]** Mandelkow *et al.* Neuroimage, **32**(3): 2006 **[6]** Mullinger *et al* Proc ISMRM 2007 #3441 [7] Allen *et al* Neuroimage **8**:229-239,1998 **[8]** Veen *et al*, IEEE Transactions on Biomedical Engineering **44**(9), 1997. **[9]** Koch *et al,* The Journal of Neuroscience **26**(18): 2006