Delayed BOLD in the somatosensory cortex and its possible relationship to beta band event related synchronisation

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Introduction: Over the past decade, studies have employed multi-modal neuroimaging in order to gain insight into the electro-physiological effects that underlie the BOLD fMRI response. Electrophysiological signals that result from EEG or MEG studies are rich in information; however some studies consider only the phase locked stimulus evoked response and its relationship to BOLD. These responses, though important, are transient (lasting ~300ms) and represent only a fraction of the electrophysiological processes that can be measured. Other studies have investigated the relationship between non-phase locked stimulus induced changes in spontaneous neural oscillatory processes. For example, in somatosensory cortex, beta-band (13-30Hz) oscillations exhibit characteristic loss in power (event-related desynchronisation, ERD) at the onset of sensory stimulation; this loss is prolonged throughout stimulation and a subsequent increase above baseline (event-related synchronisation, ERS, also known as the post stimulus beta rebound) is observed on stimulus cessation. These effects, in particular the post stimulus beta ERS, can last for up to 2s after stimulus offset. Recent work has shown a close relationship between the spatial distribution of the beta ERD and ERS, and that of BOLD [1]; here we extend this work. We use MEG to measure the temporal profile of ERD/S, however its limited spatial resolution restricts our ability to spatially separate the two effects. We therefore examine the spatial distribution of the BOLD signal using models based on the temporal signature of beta ERD and ERS. Our ERS model highlights voxels with significantly delayed BOLD responses. We speculate that such delayed responses are not simply a result of haemodynamic lag, but rather that they could be explained by a post stimulus beta band ERS.

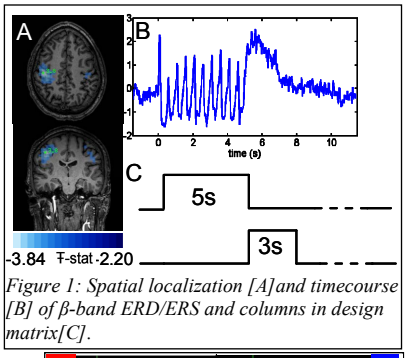

Figure 1: Spatial localization [A]and timecourse [B] of β-band ERD/ERS and columns in design matrix[C].

Methods: 8 subjects took part in parallel MEG/fMRI experiments involving non-painful median nerve stimulation. Electrodes were placed on the subject's right wrist and a 0.5ms voltage pulse was applied causing stimulation of the median nerve and flexion of the middle finger. Trains of 10 pulses were employed with Inter Stimulus Intervals (ISIs) of 0.5s. The trial length was 13s for MEG with 1.5s pre-stimulus time, 50 trials were acquired at a sample rate of 600Hz using a 275 channel CTF system. Coregistration to anatomical MRI was performed using head digitisation. MEG data were analysed using synthetic aperture magnetometry (SAM). Spatial localisation of power changes in the beta band (13-30Hz) was achieved by comparison of an active contrast window (0.5-4.5s) to a control contrast window (7.5-11.5s). Pseudo-T-stat images (1mm^3 resolution) were created showing regions of beta band power change. Timecourses of electrical activity were extracted from peaks in SAM images and Hilbert transforms applied to obtain the envelope of oscillatory activity. The resulting timecourse data were averaged across trials and subjects.

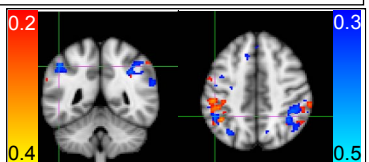

Figure 2: Normalized and averaged T score images for standard (Red) and delayed (Blue) BOLD.

In fMRI, BOLD data were acquired using a Philips 7T Achieva System (GE-EPI; TR=2200ms; TE=26ms; 2mm isotropic voxels; 192mm FOV). 21 transverse slices were acquired covering the sensorimotor cortex. Total trial length was increased to 44s allowing the hrf to return to baseline, 10 trials were acquired. Data were motion corrected, smoothed using a 3mm Gaussian kernel and processed using a GLM in SPM5 with two separate columns in the design matrix: the first representing the stimulus (block design with duration 5s corresponding to ERD); the second representing a 5s delayed temporal response with 3s duration (corresponding to ERS), based on the MEG beta band timecourse measures (see Fig.1). T score images are normalized by their peak value and averaged across subjects in MNI space. Voxels exhibiting significant correlation ($p<0.05$ FWE corrected) with the two columns were derived (we call these the standard and the delayed BOLD responses). BOLD timecourses were then extracted from 6x6x6mm^3 clusters centred on the global maxima. fMRI data were also processed using ANOVA [3]. This model free analysis allowed elucidation of voxels exhibiting a significant BOLD response at any latency. A 'time to peak' map was generated by measuring the time between stimulus offset and the peak in the hrf for all activated voxels defined by ANOVA.

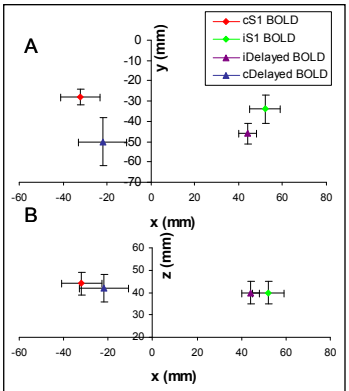

Figure 3: Averaged local maximum locations in MNI coordinates, with standard error across subjects in transverse [A] and coronal [B] planes.

Results: All 8 subjects showed significant standard BOLD responses in sensory cortex; 5 of the 8 subjects exhibited significant delayed BOLD; results presented are limited to these 5 subjects. Fig.1A shows the spatial distribution of beta ERD. Fig.1B shows the associated timecourse extracted from contralateral S1 (cS1) with beta ERD, ERS and the evoked response to the 10 individual median nerve stimuli apparent. Fig.2 shows the functional images for both standard (red overlay) and delayed (blue overlay) BOLD. Both effects appear bilaterally in S1; the activated area representing standard BOLD is larger in contralateral cortex with delayed BOLD appearing in neighbouring regions. Fig.3 shows the locations of the average maxima for standard and delayed BOLD. Note that the delayed response is posterior and medial to the standard response; both are in approximately the same axial plane. Fig.4 shows the timecourses extracted from 6x6x6mm^3 clusters in contralateral and ipsilateral cortices. Both standard and delayed BOLD responses are shown averaged across subjects. Finally, Fig.5 gives the results of our ANOVA analysis, showing the distribution of significantly active voxels as a function of their peak latency. The 'bimodel' nature suggests that there may be two separate responses which could be associated to ERD and ERS.

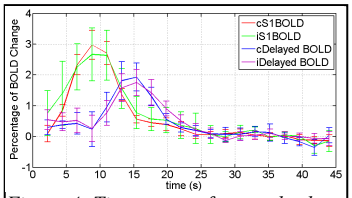

Figure 4: Timecourses for standard and delayed BOLD.

Discussion: We have investigated temporal delays in the fMRI BOLD response, with a view to investigating whether a post stimulus electrophysiological effect, beta ERS, induces a temporally delayed BOLD response. Previous work has suggested that beta band ERD and ERS may have separate neural generators; however MEG lacks the spatial resolution to investigate whether the two effects indeed arise from different cortical locations. By basing BOLD models on MEG timecourses we did find that significantly delayed BOLD responses are apparent in contralateral and ipsilateral somatosensory cortices. Although we cannot definitively link the standard BOLD with the beta ERD and evoked response, and the delayed BOLD with beta ERS, the existence of a bimodal distribution of BOLD (Fig.5) response rather than a continuous distribution lends weight to this association.

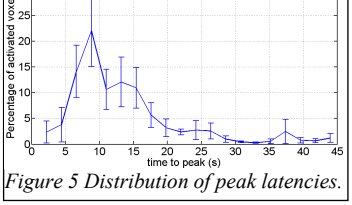

Figure 5 Distribution of peak latencies.

References: [1] Stevenson et al. Human Brain Mapping. In press (2010). [2] C. Gaetze et al., Neuroimage 30 pp899-908 (2006). [3] S. Clare et al., Magn. Reson. Med. 42 pp1117-1122 (1999).

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