Linearity of the BOLD response: A comparison between fMRI and MEG

C. M. Stevenson[1], M. J. Brookes[1], G. R. Barnes[2], A. Hillebrand[2], S. T. Francis[1], and P. G. Morris[1]

[1]Sir Peter Mansfield Magnetic Resonance Centre, School of Physics and Astronomy, The University of Nottingham, Nottingham, Nottinghamshire, United Kingdom, [2]WELLCOME Trust Laboratory for MEG Studies, Aston University, Birmingham, West Midlands, United Kingdom

Introduction: BOLD fMRI is a widely used method for exploring brain activity [1]. However, for BOLD to reach its full potential and provide a quantitative measure of brain activity, it is necessary to understand the neural basis of the response. Simultaneous microelectrode and fMRI BOLD measurements have shown that the BOLD response is best characterised by local field potentials (LFP's), which are thought to be largely synaptic in origin [2]. Since, due to their prolonged duration, synaptic processes are thought to be the basis of MEG signals, one would expect a good correlation between BOLD and MEG responses [3]. In this work, we investigate the degree to which the BOLD response reflects underlying neuronal activity. Here, the induced oscillatory response in the -band (15-30Hz) is measured by MEG and the haemodynamic response is measured by fMRI, for stimuli of varying durations. These are compared to determine whether the non-linearity commonly observed in the BOLD response reflects a non-linearity in neuronal activity, as determined by MEG, or is a consequence of haemodynamic coupling.

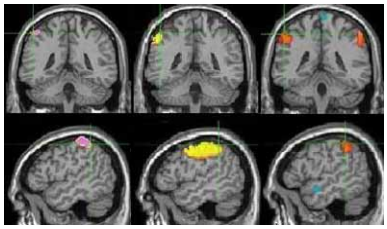

Figure 1: Spatial Localisation of MEG and BOLD data. Left: β-band ERD Tstat=1.1, Middle: β-band ERS Tstat=1.1, Right: BOLD p-corrected 0.05, Tstat=5.1.

Methodology: Four healthy subjects took part in the study. The paradigm comprised visually cued repetitive (4Hz) abductions of the right index finger. A single trial contained 2s pre-stimulus rest period, the finger movement (of duration 1s, 2s, 4s, or 6s), and a post-stimulus rest period, making each trial 12s in total. For MEG, 20 trials were recorded per stimulus duration. For fMRI, trial durations were increased to 30s and the number of trials reduced to 8 to account for the longevity of haemodynamic responses and the higher SNR in fMRI. MEG data were acquired at a sample rate of 600Hz using a third order synthetic gradiometer configuration of a 275-channel CTF system. Co-registration to anatomical MRI was performed using head digitisation (Polhemus Isotrack). MR data were acquired using a Philips Achieva 3T system running EPI (TR=2000ms; TE=45ms; 3mm^3 voxels; 192mm FOV). 18 axial slices were acquired covering motor cortex.

Data Analysis: Analysis of MEG data was carried out using Synthetic Aperture Magnetometry (SAM) [4]. For all subjects, large variations in cortical electrical oscillatory power were observed in the -band (15-30Hz). These changes comprised a loss of oscillatory power for the duration of the finger movement followed by a large increase in oscillatory power immediately following movement offset. Localisation of these beta band effects was achieved by comparing the oscillatory power during two time windows, termed the active and passive windows. In order to derive the location of the loss in oscillatory power, the active contrast window spanned the duration of stimulation and the passive window spanned the 2s prior to stimulation. Similarly, for localisation of the post movement increase in beta band power, an active contrast window spanning 2s post stimulation and the passive window spanning the 2s prior to stimulation were used. In order to identify areas of significant (p=0.05 corrected) BOLD contrast, standard regression techniques were employed using SPM. Regions of interest defined by the SAM images were used to define the location for placement of 'virtual sensors'. These virtual sensors, also derived using SAM, estimate the timecourse of electrical activity at some predefined location in the brain. A Hilbert transform was applied to the virtual sensor data allowing estimation of the envelope of oscillatory activity, which was subsequently averaged across trials. BOLD timecourses were also extracted from fMRI data using regions of interest defined from the BOLD statistical maps. Linearity of the β-band MEG response for all stimulus durations was assessed by integration of the Hilbert envelope of oscillatory power for the duration of stimulation. To assess the linearity of the BOLD response, the area under the BOLD time courses was calculated. An average signal value was calculated within the window (25s<t<30s) and used to give a baseline for integration.

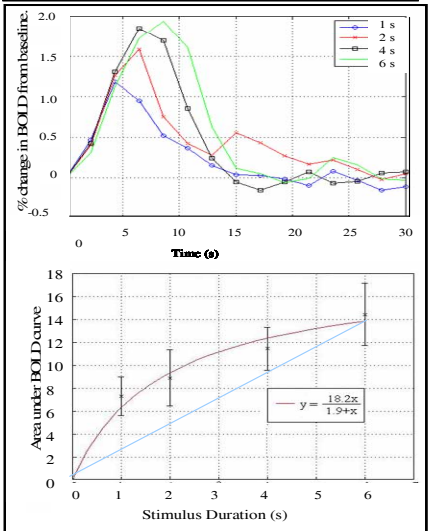

Figure 2. Top:3T BOLD time courses for stimuli of varying durations. Averaged over 4 subjects. Bottom: Area under BOLD curves with respect to stimulus duration.

Results and Discussion: The good spatial correlation between β-band activity and the fMRI BOLD response, shown in Figure 1 suggests that the two measurements are closely related. Both localise to the contra-lateral primary motor cortex and on lowering the statistical threshold ipsi-lateral activity also becomes apparent. The post movement rebound is found slightly anterior to the movement related desynchronisation. The BOLD time courses (Figure 2a) behave largely as predicted, with time courses for stimuli of longer durations peaking later. It is clear from Figures 2a and 2b that the BOLD response is non-linear with respect to stimulus duration, with the responses for shorter stimulus durations being underestimated by a simple linear model (shown in blue). The MEG β-band response is well documented and the results presented behave as predicted. This can be seen in Figure 3, with the MEG response shown in blue alongside an overlay of the corresponding BOLD response shown in red. In assessing the linearity of the MEG response, the total power loss during stimulus presentation was calculated and the results are shown in Figure 4. It can be seen that the β-band power loss increases roughly linearly with stimulus duration and does not show the same non-linearity as the BOLD response. It should be pointed out however that no trend is apparent in the linearity of the post-movement rebound. The linear response of the β band loss in power and the non-linear BOLD response would imply that either non-linearities in BOLD are primarily haemodynamic in origin, or they reflect non-linearity in other aspects of the neuromagnetic response such as the beta rebound, or phase locked transient or sustained effects. It is somewhat counter intuitive that a β-band power decrease should lead to an increase in energy demand and therefore the BOLD response. However, this MEG derived response reflects a change in state of a large population of neurons and so could still be linked to increases in metabolic activity.

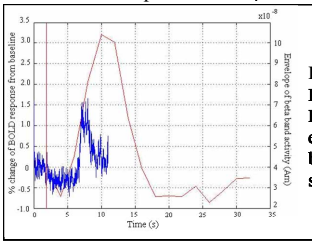

Figure 3: An overlay of the BOLD timecourse and the Hilbert transform of the virtual electrode trace from the peak of beta band activity for the 4sec stimulus.

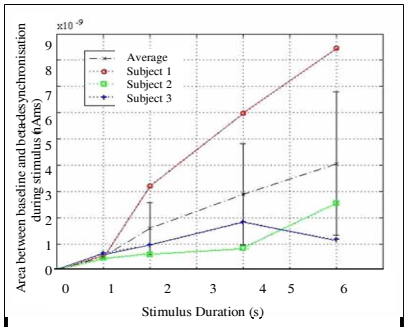

Figure 4:Area of the Hilbert envelope of beta-band desynchronisation for varying stimulus duration.

References: [1]Ogawa, S. et al., *Magn. Reson. Med*., **14**, 68 -78 (1990). [2] Logothetis, N.K. et al., *Nature*, **412**, 150-157 (2001). [3] Kaufman, L., et al., Magnetic Source Imaging of the human Brain, Lawrence Erlbaum Associates Inc., 2003. [4] Robinson, S.E. and Vrba, J., Functional Neuroimaging by Synthetic Aperture Magnetometry(SAM), *Biomag98, 11th Int. Conf. On Biomagnetism*.(1998).