Neuromagnetic correlates of the 7T BOLD Response in Visual Cortex

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Introduction: Recent studies [e.g. 4] have shown that a combination of functional magnetic resonance imaging (fMRI) and magnetoencephalography (MEG) may provide insight into the neuronal basis of the BOLD effect. The neuromagnetic field measured in MEG is thought to be largely induced by post-synaptic currents in the dendrites of active, cortical pyramidal cells. Attwell and Laughlin [1] have argued that the majority of energy expended in the human brain is also related to post synaptic events, suggesting that if the fMRI BOLD response is truly a measure of energy uptake in the brain, it should correlate strongly with the measured neuromagnetic response in MEG. Logothetis *et al* [2] have shown, using invasive microelectrode recordings in primates, that a 40-130Hz signal is detectable from primary visual cortex in response to visual stimulation. This signal, termed the local field potential (LFP), was said to demonstrate a stronger correlation with the BOLD response than the higher frequency (~300-1500Hz) multi unit activity (MUA) also detected. Since LFP is largely postsynaptic, this further supports the idea that MEG and BOLD are comparable. Here, we show that neuromagnetic signals in the 55 – 80Hz band correlate with the BOLD response for a visual stimulus. Further, we assess the linearity of the MEG and BOLD responses to visual stimuli of varying contrasts.

Methods: Three healthy volunteers took part in the study. The visual stimulus comprised a simple drifting grating (drift frequency 8Hz, 6° visual angle) presented centrally in the visual field. Five stimuli were presented of varying contrast (0, 0.125, 0.25, 0.5 and 1). FMRI experiments comprised 6 trials per contrast, each trial being 30s in duration. MEG experiments comprised 20 trials per contrast, each 8s in duration. A longer trial length was used in fMRI to allow the haemodynamic response to decay back to a baseline state.

FMRI data were acquired using a Philips 7T Achieva system. EPI images were collected from 18 contiguous axial slices the covering visual cortex (TE=25ms, TR=2s, matrix size 64x64, voxel size 2x2x2mm^3). Statistical images showing areas of maximum BOLD contrast were created using standard techniques in SPM.

MEG data were recorded using a 275 channel CTF system with a sample rate of 600Hz using a third order gradiometer configuration. Source space analysis was undertaken using the MEG beamformer approach. Pseudo-T-statistical volumetric maps [3] showing the spatial distribution of stimulus related oscillatory power change in the gamma (55-70Hz) band were produced and compared to those showing BOLD contrast.

Regions of interest were derived based on the closest corresponding areas of activation in the MEG and fMRI statistical maps. In all subjects these regions lay in and around the calcarine fissure. Timecourses showing changes in gamma band power, and the BOLD haemodynamic response were then extracted. MEG timecourses were obtained by taking the Hilbert transform of the beamformer derived virtual sensors traces [3]. For all five contrasts, the contrast response was calculated by integration of the Hilbert envelope of gamma band power (for MEG) and integration of the BOLD response (for fMRI).

Results: Figure 1 shows a spatial comparison of the areas of significant (T>6) BOLD contrast, and areas of significant (Ŧ>6) change in gamma band activity for a single subject. For all subjects spatial agreement between gamma band change and the BOLD response was good and the average (across subjects) discrepancy between the centre of mass of the gamma band change and the BOLD response was 10(±5)mm. Such differences might be accounted for by errors in co-registration between MEG and MRI. Figure 2 shows the contrast response functions for fMRI in the left hand plot and MEG in the right hand plot. Both the BOLD and neuromagnetic responses increase with contrast and appear to saturate for high contrasts. Figure 3 (A – E) shows the timecourses of the BOLD HRF together with the associated increase in gamma band activity. Again it is clear that both the HRF amplitude and the gamma band change increases with stimulus contrast. Figure 3F shows the integrated contrast response functions derived from both fMRI and MEG plotted against one another. Despite the small number of subjects, this plot suggests an approximately linear relationship between them.

Discussion: The results show that a strong correlation exists between BOLD fMRI and the gamma band neuromagnetic response detected in MEG. We have also shown that the response to visual stimulation at varying contrasts is largely similar in both MEG and fMRI. This data adds further weight to the argument that MEG and fMRI are intimately linked, both being reflective of the same postsynaptic activity in primary cortices. The results presented here are also in strong agreement with the invasive studies by Logothetis *et al* and we suggest that the gamma band response in MEG may be the human equivalent of the LFP response detected in monkeys.

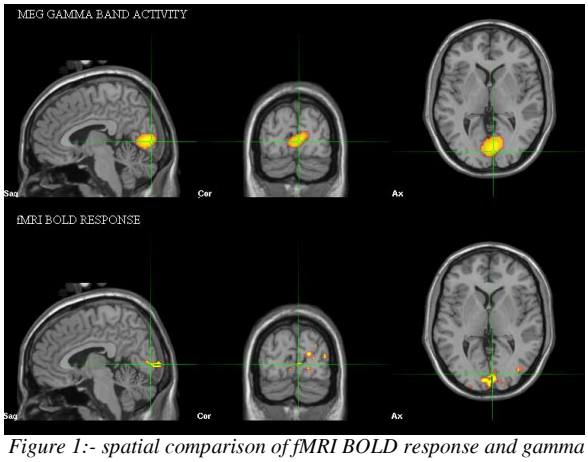

Figure 1:- spatial comparison of fMRI BOLD response and gamma band activity in MEG.

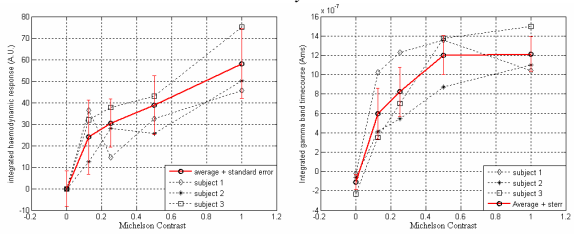

Figure 2:- Contrast response functions in fMRI (left) and MEG (right). Individual subjects and group average shown.

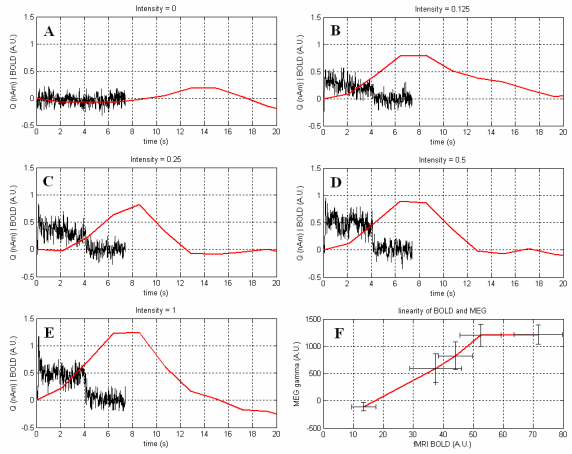

Figure 3:- MEG (black) and fMRI (red) timecourses. A: Contrast = 0; B: Contrast = 0.125; C: Contrast = 0.25; D: Contrast = 0.5; E: Contrast = 1; F: integrated MEG and fMRI responses plotted against one another. In all cases group averages are shown.

As well as the non-phase locked response in the gamma band shown here, other MEG responses are detectable [4], e.g. loss of power in the alpha (8 – 13Hz) band and phase locked evoked responses. These effects may also be strongly associated with the BOLD effect and should be the topic of future study.

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References: 1) Attwell and Laughlin, J. Cerebral Blood Flow and Metabolism 21 (1133-1145), 2001. 2) et al, Nature 412 (150-157) 2001. 3) Vrba and Robinson Methods, 25 (2) 249-271, 2001. 4) Brookes et al, Neuroimage 26 (302-308) 2005.