Neuronal Basis of the BOLD Effect Investigated Using Magnetoencephalography

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Introduction: Recent studies 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 [(1)]. Our own studies [(2)] have shown that in response to visual stimulation, alpha band desynchronisation, gamma band synchronization, and sustained evoked responses are detectable using MEG, and furthermore, each of these neuromagnetic effects appears to overlap spatially with the BOLD response. In this current study, we extend our previous work by the use of a quarter field visual stimulus in order to prevent field cancellation of neuromagnetic effects across the calcarine fissure, and hence allow more accurate source space localisation in MEG. By characterization of the detected signals in sensor space, we show that the three neuromagnetic effects have different origins, and thus will contribute separately to the energy demand believed to underlie the BOLD signal.

Methods: In both fMRI and MEG experiments 3 healthy volunteers were presented with a quarter field visual stimulus. This comprised a checkerboard pattern presented in the subject's lower right visual field. Literature [(3)] suggests that due to the partial decussation of the optic nerve, lower right quarter field visual stimulation should lead to cortical activity in only the left primary visual cortex. FMRI experiments comprised 10 trials, each 30s long. MEG experiments comprised 40 trials, each 14s long. A longer trial length was used in fMRI to allow the haemodynamic response to decay back to a baseline state. In both MEG and fMRI, five separate stimulus durations were used (500ms, 1s, 2s, 4s, and 8s).

FMRI data were obtained using a 3T MRI scanner, with custom-built head gradient coil and a whole head TEM RF coil. MBEST EPI images were collected from 10 contiguous coronal slices at the back of the head (TE=40ms, TR=1s, matrix size 64x64, voxel size 4x4x6mm^3). Images were processed using standard techniques in SPM99 [(4)]; co-registration of SPM's onto anatomical images was achieved using AIR registration in MEDx (Sensor Systems).

MEG data were recorded using a 151 channel CTF Omega system with a sample rate of 625Hz using a third order gradiometer configuration. Source space analysis was undertaken using the MEG beamformer approach in conjunction with the general linear model[(5,6)] to create T-statistical volumetric maps showing the spatial distribution of both stimulus related oscillatory power change (in the gamma (55-70Hz) and alpha (8-13Hz) bands), and the sustained field effect. In addition to this source space analysis, the distribution of neuromagnetic effects was also mapped spatially in sensor space, by use of the same GLM metric on individual channel signals.

Results: Figure 1 shows the spatial distribution of the BOLD effect, alpha band desynchronisation, gamma band synchronization, and the sustained field for a single representative subject at 4s duration. (MEG statistical maps are thresholded at $p_{UNCORRECTED}$, = 0.001; BOLD statistical maps are thresholded at $p_{CORRECTED}$ = 0.05.) Figure 2 shows the spatial distribution of the same neuromagnetic effects mapped in sensor space, (using the same subject and all durations). These statistical maps are thresholded at $p_{UNCORRECTED}$ = 0.01. (In the sensor space maps, blue represents a decrease in oscillatory power, and red an increase. In the case of the sustained field, the red overlay simply represents the presence of a sustained field.) Figure 3 shows the temporal response of the sustained field (blue), gamma band synchronization (green), and BOLD effect (red) for the 4s duration stimulus.

Discussion: At first sight, these results seem contradictory. The GLM / beamformer method[(6)] appears to localize gamma band synchronization, and sustained fields to the same location in source space. However, the field maps clearly show that the sustained field and gamma ERS are detected at different locations in sensor space. There are two plausible explanations for this. Firstly, the two current sources may have the same origin, but differ in orientation. Secondly, the two sources could differ in spatial extent. In either case, localisation of the centre of activation foci in source space will be accurate to within the limitations of the beamformer assumption set [(5)]. The difference in field maps for the sustained field and gamma signals shows conclusively that gamma band ERS, and sustained field are fundamentally different in origin, and hence each will have its own implications in terms of the BOLD effect.

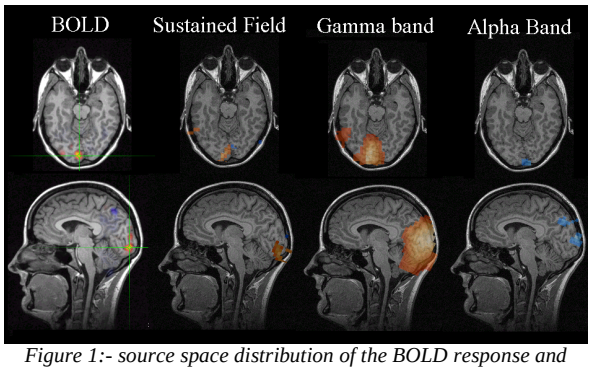

Figure 1:- source space distribution of the BOLD response and neuromagnetic effects

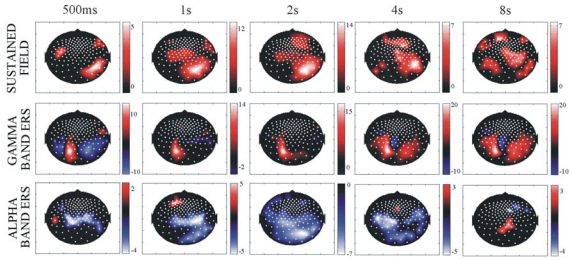

Figure 2:- Sensor space distribution of the three neuromagnetic effects for all five stimulus durations

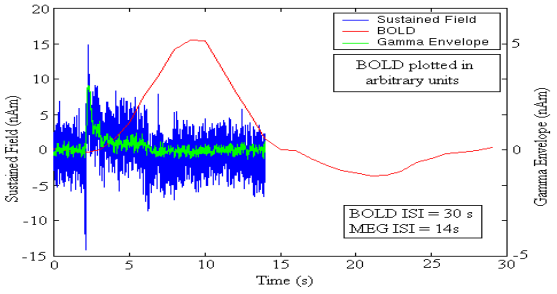

Figure 3:- Time course for the 4s duration data.

Logothetis *et al* [(7)] have shown that, using invasive microelectrode recordings in primates, a 40-130Hz signal is detectable from primary visual cortex. This signal, termed the local field potential (LFP), was said to demonstrate a stronger correlation with the measured BOLD response than the higher frequency (~300-1500Hz) multi unit activity (MUA) also detected. The gamma band (55-70Hz) activity, demonstrated here using MEG represents (at least in part) an equivalent to the LFP signal in the human primary visual cortex. Its spatial distribution is (both across stimulus durations, and subjects) robustly correlated to the BOLD response, and time course plots of gamma band power averaged across trials (see figure 3) demonstrate that a significant gamma response exists throughout visual stimulation, again equivalent to the Logothetis observation. Both in terms of its underlying physiology, and its relationship to the BOLD response, the sustained field response is less well understood. In these results its spatial correlation to the BOLD response is less robust across subjects and stimulus durations. However this may be due to the low frequency noise making its detection using MEG difficult. One may however speculate that the sustained field could represent the summation of asynchronous electrical activity of neuronal networks. Unlike the gamma and sustained field effects, alpha band desynchronisation, though always present, showed variability both across subjects and durations.

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References: 1) Singh et al, Neuroimage 16 (103-114), 2002. 2) Brookes et al, Proc. ISMRM, Kyoto, (abs No 207) 2004. 3) Bear, Connors and Paradiso, Neuroscience 2nd Ed. Lippincott Williams and Wilkins 2001. . 4) Worsley and Friston, Neuroimage 2 (173-181), 5) Van Veen et al, IEEE Transactions on Biomedical Engineering 44(9), 1997. 6) Brookes et al, Neuroimage 23 (936 – 946) 20041995. 7) Logothetis et al, Nature 412 (150-157) 2001.