New Processing Methods for Magnetoencephalographic (MEG) Data Reveal Neuronal Correlates to the BOLD Response

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Introduction: The fMRI BOLD response is driven by a local increased energy demand in active neural tissue, and a recent study (1) has suggested that ~74% of this increased demand for energy results from postsynaptic events. Recordings of electrical activity made using magnetoencephalography (MEG) have also been shown to be due to postsynaptic currents (9), and therefore a direct link between the MEG and fMRI BOLD response may be postulated. This relationship has been probed using MEG beamformer based analyses (3,4,5). A beamformer is essentially spatial filter optimally tuned to a particular location within the brain. By projecting raw MEG data through a collection of spatial filters, estimates of changes in electrical activity brought about by some external (or internal) stimulus can be made at chosen locations in the brain, allowing the construction of volumetric images of neuronal activity change (4). In this work, we outline a method for application of the General Linear Model (GLM) (6) to MEG beamformer analysis. We demonstrate that application of our novel technique to raw MEG data can highlight spatiotemporal correlates of the BOLD response, shedding new light on the relationship between fMRI BOLD and neuronal activity. Our method is tested on simulated data and applied to a somatosensory dataset to reveal correlation between BOLD and a sustained field.

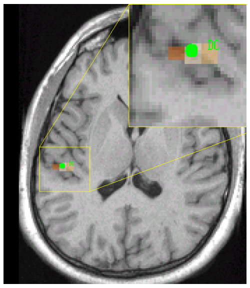

Figure 1: - Result of simulations, Red overlay shows volumetric image, green marker gives simulated DC source position. Inset:- Enlarged version.

Theory: Mathematically, a beamformer spatial filter, tuned to location θ, takes the form of a weights vector, $\underline{W}_\theta$, which is defined such that the electrical source strength $y_\theta(t)$ at time t is given by (5):

$$y_\theta(t) = \underline{W}_\theta \underline{m}(t) \qquad [1]$$

Where $\underline{m}(t)$ is the instantaneous vector of field measurements across the scalp at time t. By sequential application of equation 1 to all time samples in an MEG dataset it is possible to construct a vector time course, $\underline{y}_\theta$, of source strength for location θ (commonly termed a virtual electrode). If temporal patterns of activation (e.g. a sustained field) are known *a priori*, then these effects can be modeled using the GLM, which states (6):

$$\underline{y}_\theta = \underline{\underline{G}}\,\underline{\beta}_\theta + \underline{e} \qquad [2]$$

Where $\underline{\underline{G}}$ represents the design matrix and has a single column for each effect modeled. The vector $\underline{\beta}_\theta$ contains a single parameter representing the presence of any modeled effect in the timecourse and $\underline{e}$ represents thermal noise in $\underline{y}_\theta$. Estimates of $\underline{\beta}_\theta$ and its associated error allow for computation of a T-score and hence formulation of volumetric images.

Methods: MEG data were simulated using the configuration of a 151-channel Omega system (CTF Systems Inc.) and a source space based on the head shape of a single subject, measured during an experimental recording session. A single dipolar source was simulated on the cortical surface with orientation perpendicular to the cortical surface. This source was designed to emulate a sustained field response previously observed experimentally in somatosensory cortex (8). Its time course followed a simple DC step function, 'on' for duration 1.1s with amplitude 2nAm. Simulated physiological and thermal noise was added to the source and the forward problem solved using the method of Sarvas et al (2). The GLM-beamformer method described above was then employed to locate the simulated source.

The same GLM-beamformer algorithm was applied to MEG data from a somatosensory stimulation experiment to look for a sustained field response in somatosensory cortex. Data were recorded on a 151-channel Omega system (CTF Systems Inc.), at a sample rate of 625Hz in 40 18s epochs. 200Hz somatosensory stimulation was applied to the subjects' right thumb via a piezoelectric crystal. Epoch's consisted of 2s prestimulus baseline followed by 8s stimulation and 8s rest period. Volumetric T-statistical images, created using the GLM beamformer method, were overlaid onto the individual subject's anatomical MRI image. Co-registration to the anatomical image was achieved using Align (10). These results were compared to a similar fMRI experiment. The same 200Hz stimulation being applied for a similar duration to the subjects right thumb (The post stimulus rest period was extended in fMRI to allow for the decay of the HRF back to baseline). MBEST ERI images (TE = 40ms, TR = 100ms, matrix size 64x64, with resolution 3x3x4mm^3) were recorded on a 3T MRI scanner using a custom-made short head gradient coil and RF surface coil. FMRI data were processed using standard techniques in spm99.

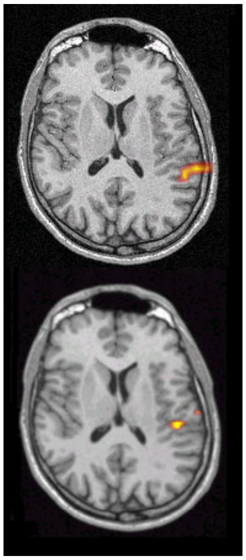

Figure 2: - Single subjects result from the somato-sensory experiment: Top: Spatial distribution of the sustained field. Bottom: The spatial distribution of the BOLD effect.

Results and Discussion: Figure 1 shows the results of the simulation. The red overlay shows the volumetric T-statistical image from the GLM-beamformer method and the green marker shows the exact position of the simulated DC source. The method used localized the source to within an error of <5mm, the resolution limit of the beamformer used. Figure 2 (top) shows the spatial distribution of the sustained field in somatosensory cortex with the functional image thresholded at a T-score of 5. Figure 2 (bottom) shows the equivalent BOLD image to a corrected p-value of 0.05.

In this study we have shown that the application of the general linear model to MEG beamformer images can be successfully used to map the spatial distribution of a sustained field effect both in simulated and real data. Our somatosensory investigation also shows that within the resolution limits of the techniques used, the sustained field may be a spatial covariate of the BOLD signal, (a discrepancy in position of ~1.5cm between BOLD activation and the sustained field was thought to be a result of co-registration errors). Application of our method extends beyond this simple application. By employing the Hilbert transform to a virtual electrode timecourse, the GLM method can be used to obtain images of gain or loss of oscillatory power in any given frequency band. This method will allow for statistical mapping of oscillatory cortical electrical activity and its spatial relationship to the fMRI BOLD response may therefore be probed. By plotting virtual electrode time courses the temporal relationship between electrical activity and the haemodynamic response may also be investigated

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