A comparison of quantitative perfusion measurements and MEG phenomena

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Introduction: Previous studies correlating MEG responses with fMRI have investigated the coupling with the BOLD response. However, the BOLD signal originates from a complex interaction of cerebral blood flow, cerebral blood volume and oxygen consumption changes. Arterial Spin Labeling (ASL) techniques provide a quantitative measurement of local tissue blood flow, and this may be more directly related to neuronal activation, as measured by MEG, than BOLD [1]. Here, we investigate the correlation between evoked and induced MEG signals and the changes in cerebral blood flow (CBF), together with the T2* and BOLD, for a simple visual stimulus. The linearity of the responses to visual stimuli of varying contrasts is assessed for each to provide insight into neurovascular coupling mechanisms.

Methods: Four healthy subjects took part in the study. The visual paradigm comprised a sinusoidal drifting grating, presented in a circular window in the lower left hand quadrant of the visual field with a visual angle of 5°. Five Michelson Contrasts (0, 0.125, 0.25, 0.50 and 1) were presented pseudo-randomly with stimulus duration of 4 s for MEG and 10 s in ASL. To maintain attention, on stimulus cessation, subjects executed a button press to indicate the contrast of the stimulus. Trial length was 8 s in MEG with 20 trials per contrast and 26 s in fMRI, with 12 trials per contrast. MEG data were acquired at a sample rate of 600Hz, on a 275-channel CTF system. Co-registration to anatomical MRI was performed using head digitisation (Polhemus Isotrack). Contiguous axial slices covering the visual cortex were acquired on a 3T Philips Achieva system using QUIPSSII [1] (TI1=700ms; label delay=1400ms; TR=2000ms, Double echo acquisition TE=16,40 ms, 3x3x5mm3 voxels, 192mm FOV, 5 slices, SENSE factor 2). T1, T2* and Mo maps were acquired in the same scan session for quantification purposes.

Data Analysis: MEG data were analysed using synthetic aperture magnetometry (SAM) [2]. Spatial localisation of oscillatory power changes in the beta (15-30Hz) and gamma (60-80Hz) bands was achieved by comparison of an active contrast window of 0-3.9s to a passive contrast window of 4.1-7.9s. Pseudo T-stat images (1mm3 resolution) were created showing regions of activity within these bands. Virtual sensor traces were extracted from peaks of activity in the SAM images to show time courses of oscillatory power. These were obtained by applying a Hilbert transform to the virtual sensor data and averaging across trials. Linearity of the response was assessed by integration of the Hilbert envelope. An average signal value taken over the rest period was used as the baseline for integration. Areas of significant (p=0.05 corrected) activity in fMRI CBF, BOLD and T2* data were identified using SPM5. 9x9x9mm cubic volumes surrounding the global maxima were used to obtain average time-courses of the haemodynamic response. Linearity of the fMRI responses was assessed by integration of the time course. An average signal value during the 0 contrast stimulus was computed and taken to be the baseline for integration. CBF quantification was achieved using a single compartment model [1]. Modulations in CBF with contrast were measured by taking the maximum CBF value at each contrast and averaging across trials and subjects.

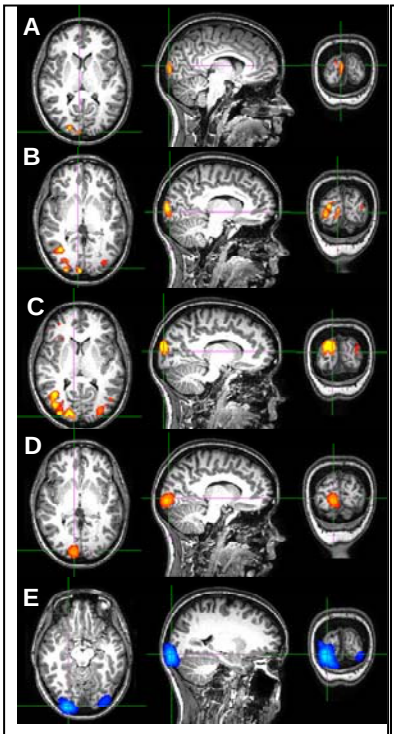

Figure 1: Spatial localization of fMRI and MEG effects in a single representative subject.[A] ASL, [B] T2*, [C] BOLD (p<0.05 corrected), [D]

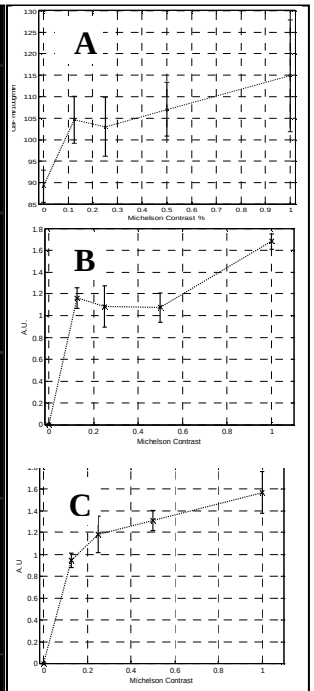

Figure 2: Average contrast response curves with standard error. [A] Maximum values of CBF at each contrast [B] T2* and [C] BOLD.

Response	Contra-lateral peak locations	Ipsi-lateral peak locations
MEG β ERD (15-30Hz)	[33±2, 19±2, 40±4]	[61±2, 19±1, 38±2]
MEG γ ERS (60-80Hz)	[40±1, 19±1, 40±1]	No response
BOLD	[34±2, 19±1, 39±5]	[63±5, 29±8, 42±3]
ASL	[35±5, 20±2, 38±4]	No response

Table 1: Average peak locations of MEG and fMRI responses are shown in standard space with associated standard error.

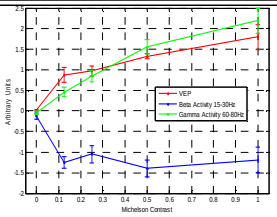

Figure 3: Average contrast response curve with standard error for MEG responses in the β band (blue) γ band (green) and visual evoked field.

Results and Discussion: Figure 1 demonstrates the excellent spatial co-localisation of the fMRI responses and MEG responses. Both localise to the contra-lateral central visual areas, with activity of lower T-stat in the ipsi-lateral and more lateral visual areas. Table 1 shows a spatial separation in the maxima of the ASL data and the BOLD data. The lack of bi-lateral activity in ASL may be due to a lower signal to noise ratio than BOLD, rather than a difference in the underlying response. The spatial separation of the ASL and BOLD peaks results from ASL being sensitive to inflow arterial blood whereas BOLD is venous weighted and draining vein effects may dominate. Figure 2 shows the contrast response curves for the ASL, T2* and BOLD data. The differences in the shapes of the curves reflect the differing functional roles of the responses. The absolute values of CBF shown in Figure 2A show a more monotonic increase in amplitude with increasing stimulus contrast and follow a similar trend to the visual evoked field and gamma. The visual evoked field shown in Figure 3 exhibits a linear response to contrast, as has previously been shown in MEG studies [3]. The gamma response exhibits a similar trend and does not seem to saturate at high contrasts. This is analogous to the contrast tuning of the BOLD response shown in Figure 2C. The beta response does not change with contrast, this may reflect of an idling rhythm with a threshold on/off.

Conclusion: The striking spatial co-localisation of two disparate phenomena (electromagnetically based oscillatory activity and fMRI based) indicates that electrical effects measured by MEG, the fMRI BOLD response and cerebral perfusion, as measured by ASL, are intimately related. Spatial separation of ASL and BOLD peaks along with differences in the shape of the contrast response curve, suggests a decoupling of local perfusion and activity measured with BOLD. In the four subjects studied here BOLD data appears to be spatially more closely linked to β ERD, with both responses showing bi-lateral activity. Spatial localisation of the ASL data on the other hand appears to be closer to γ activity. However, further subjects will be investigated to determine the significance of this preliminary result.

References: [1]E.C. Wong et al. MRM (1998) 39:702-708 [2]S.E. Robinson et. al., Biomag 98, 11th Int Conf on Biomagnetism, 1998. [3] S.Hall et al., NeuroImage, 26(1)(2005)13-17.