The relationship between 7T fMRI BOLD and MEG derived γ activity

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Introduction: The move to high field imaging is thought to be very beneficial for fMRI, promising an improved signal to noise ratio and increased BOLD contrast alongside increased spatial specificity [1]. It has been shown that the field strength dependence of the fractional signal change varies depending on the relative contributions of capillary and non-capillary venous vessels, with an increase proportional to $B_0^2$ for large vessels (venous and veins; $d>10\mu m$) and $B_0^3$ for small vessels (capillaries; $d<10\mu m$) [2]. Therefore, in moving from 3T to 7T one would expect an increase in the amplitude of the measured BOLD response, with an increase in weighting towards small vessels at 7T. It has been suggested that this makes BOLD data acquired at higher field strengths closer to the true site of neural activation as it is less dominated by draining veins. This increase in spatial specificity should also result in a response amplitude more closely related to true neuronal activity. MEG provides a non-invasive, direct measure of neural activity and previous studies have shown a good correlation between fMRI BOLD data and time-locked, non-phase locked oscillatory effects in MEG, particularly in the γ (60-80Hz) range [3]. Here, the induced oscillatory response in the γ-band is measured by MEG and the haemodynamic response is measured by fMRI at both 3T and 7T. The degree of modulation in gamma band activity due to a visual stimulus of varying contrast is compared to the variations in BOLD response at the two field strengths in order to determine whether 7T BOLD data is more closely related to the underlying BOLD gamma band. Virtual sensor traces were located in peaks of activity in the SAM images and time series centred on the global maxima were used to obtain average time-courses of the haemodynamic response. BOLD derived contrast response curves were obtained by integration of the BOLD timecourse. Contrast to noise ratio was computed for significantly active voxels acquired during the 100% Michelson contrast condition. The 0% contrast trials formed the baseline and the variance of this signal was taken to be the noise variance. CNR was the difference in MR signal between active and baseline states and N is the noise variance of the voxel in question. Given the difference in voxel size at 3T and 7T, with a voxel volume of 8\(\mu\)m³ at 3T being employed at 7T in comparison to 27\(\mu\)m³ at 3T, it is difficult to directly compare CNR. However, it has been assumed here that if similar values of mean CNR are achieved at both field strengths, then any reduction in activated volume is due to underlying physical differences in the signal rather than signal to noise differences. For ease of comparison, values were converted to volume of activation with a given CNR by multiplying the number of voxels with each CNR by the voxel volume used at each field strength. MEG data were analysed using synthetic aperture magnetometry (SAM) [4]. Spatial localisation of activity was achieved by integration of the SAM timecourses in a circular window in the lower left hand quadrant of the visual field with a visual angle of 5°. Five contrasts (0, 0.125, 0.25, 0.5 and 1) were presented pseudo-randomly, with the stimulus presented for 4secs. Trial length was 8secs in MEG and 16 secs in fMRI. Experiments consisted of 20 trials per contrast in MEG and 8 trials per contrast in fMRI. 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 both 3T and 7T Philips Achieva systems running GE-EPI (3T: TR=2000ms, TE=40ms, 3x3x3\(\mu\)m³ voxels, 192mm FOV, 18 slices, SENSE factor 2) (7T: TR=2000ms, TE=25ms, 2x2x2\(\mu\)m³ voxels, 156mm FOV, 15 slices, SENSE factor 1.5). Data Analysis: Areas of significant (p=0.05 corrected) BOLD contrast were identified using SPM5. 9mm³ cubic regions centred on the global maxima were used to obtain average time-courses of the haemodynamic response. BOLD derived contrast response curves were obtained by integration of the BOLD timecourse. Contrast to noise ratio was computed for significantly active voxels acquired during the 100% Michelson contrast condition. The 0% contrast trials formed the baseline and the variance of this signal was taken to be the noise variance. CNR was computed using $\frac{S}{\sqrt{N}}$, where $S$ is the difference in MR signal between active and baseline states and $N$ is the noise variance of the voxel in question. Given the difference in voxel size at 3T and 7T, with a voxel volume of 8\(\mu\)m³ at 3T being employed at 7T in comparison to 27\(\mu\)m³ at 3T, it is difficult to directly compare CNR. However, it has been assumed here that if similar values of mean CNR are achieved at both field strengths, then any reduction in activated volume is due to underlying physical differences in the signal rather than signal to noise differences. For ease of comparison, values were converted to volume of activation with a given CNR by multiplying the number of voxels with each CNR by the voxel volume used at each field strength. MEG data were analysed using synthetic aperture magnetometry (SAM) [4]. Spatial localisation of activity was achieved by comparison of oscillatory power in an active contrast window, spanning the stimulus presentation time (0.1-4s), and a passive time window spanning the post-stimulus rest period (4.1-8s). Pseudo T-stat images [4] (1mm³ resolution) were created showing regions of activity within the γ band. Virtual sensor traces were located in peaks of activity in the SAM images and time courses of electrical oscillatory power were obtained by applying a Hilbert transform of the virtual sensor data and averaging across trials. Modulation of the γ response was assessed by integration of the Hilbert envelope. MEG derived contrast response curves were correlated with the respective BOLD contrast response curves obtained at both field strengths on a subject by subject basis. Results and Discussion: Figure 1 shows a compelling agreement in spatial localisation of the peaks in γ band activity and BOLD data for both 3T and 7T experiments. A single peak of γ activity, depicted by an increase in power during stimulation, was found in all four subjects in central visual areas, contra-lateral to stimulus presentation. This was spatially coincident with the global maxima in BOLD data. Significant BOLD activity was also seen at both 3T and 7T bilaterally and in more lateral visual areas responsible for motion encoding. As can be seen in Figure 1 the 7T data is the more focal of the two responses, with a volume of significant activity of 570±120mm³ in comparison to 890±480mm³ at 3T. This is also reflected in Figure 2 which shows a smaller total volume of significant activity at 7T, but similarly mean CNR values (4.97 at 3T and 4.78 at 7T), suggesting that despite the smaller voxel volume used at 7T, the difference in volume of activation is not due to differences in signal to noise ratio. Figure 3 shows the correlation coefficient between the contrast response curve derived using the electrical oscillatory activity and the BOLD derived contrast response curves at 3T and 7T, with all four subjects showing an increase in correlation with the 7T BOLD data. The average correlation coefficient at 3T was 0.5±0.2 and 0.8±0.1 at 7T with the level of significance of the increased correlation at 7T being p=0.068.

Conclusion: The co-localisation of BOLD peaks and peaks in γ activity strongly suggests that these processes are intimately linked. The increased spatial specificity of 7T BOLD data in comparison to 3T data is demonstrated. A similar mean CNR in the two data sets suggests that the reduction in the volume of significant activity at 7T is due to an increased weighting towards small vessels rather than differences in signal to noise ratio. The increase in correlation between the gamma band contrast response curve and the 7T contrast response curve suggests that the due to the increased spatial specificity of the 7T BOLD data and the reduction in venous weighting, the resulting haemodynamic response has an amplitude more closely related to the neuronal activity than BOLD data measured at 3T.