Do neural oscillations underlie haemodynamic functional connectivity measurements?

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Introduction: In recent years, interest has increased in studying stimulus-independent, spontaneous fluctuations in BOLD fMRI signals. Resting state BOLD signals from functionally related brain areas have been shown to be correlated, implying that brain activity in these areas is linked even in the absence of a stimulus[e.g. 1]. To date, a number of data driven techniques (e.g. seed correlation, ICA) have been employed and this has lead to elucidation of approximately a dozen consistent resting state brain networks. Unfortunately, connectivity based on BOLD fMRI are confounded by non-neuronal physiological signals (e.g. cardiac and respiratory effects)[2, 3], and it remains unclear how much resting state BOLD signal correlation is due to correlated neural activity, and how much is due to non-neuronal physiological factors. The ability to investigate the neural mechanisms underlying haemodynamic connectivity measurements is therefore of great importance. Insight into the neural mechanisms underlying BOLD connectivity has been gained using concurrent electroencephalography (EEG)/fMRI[4]. Such studies have shown that fluctuations in the power of ongoing neural oscillations in the alpha (8-13Hz) and beta (13-30Hz) frequency bands correlate temporally with haemodynamic effects. Unfortunately, the poor spatial specificity of EEG makes independent spatial correlation of electrical and haemodynamic connectivity difficult. In this work, we employ magnetoencephalography (MEG) and 7T BOLD fMRI to independently measure the spatial signature of connectivity in the sensorimotor network. MEG has better SNR than EEG (due to an increased number of sensors) and since magnetic fields are not distorted by the inhomogeneous conductivity profile in the head, spatial specificity is also improved. We show that sensorimotor cortex connectivity can be identified using fMRI and MEG with good cross-modal spatial concordance. These results support previous EEG/fMRI work and the hypothesis that neural oscillations underlie functional connectivity (FC).

Methods: Four healthy, right-handed participants took part in the study which was approved by the local ethics committee. Two separate experiments were run in both fMRI and MEG. The first comprised a cued finger movement task and was used to localise the sensorimotor cortex. The second comprised a 5 minute resting state experiment during which subjects lay in the scanners, relaxed, with their eyes open. BOLD fMRI data were acquired using a 7 T Philips Achieva MR system. 24 contiguous echo planar images (TR/TE 1500/25ms, 1.5x1.5x3mm^3 resolution, 198x192x72mm^3 FOV, SENSE factor 3) were acquired giving whole brain coverage. Homogeneous B_0 was achieved using a parcellated shimming procedure. MEG data were acquired using the third order gradiometer configuration of a 275 channel CTF MEG system at a sample rate of 600Hz. Co-registration of MEG sensor space data to anatomical MRI was achieved using head digitisation (Polhemus Isotrack).

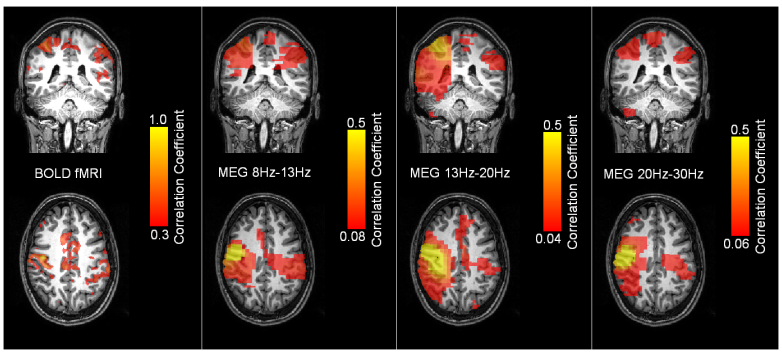

Figure 1: Connectivity maps acquired using fMRI and 8-13Hz, 13-20Hz and 20-30Hz MEG resting state data

Data Analysis: All fMRI data were motion corrected using SPM5, corrected for respiratory and cardiac artifacts using RETROICOR, and smoothed spatially using a 3mm FWHM Gaussian kernel. The sensorimotor regions were localised using data from the finger movement paradigm which were processed using a GLM (SPM5). The right primary sensorimotor cortex was selected as a seed region for further analysis. The resting state BOLD signal from the seed region (averaged over the peak voxel and its 8 nearest neighbours) was extracted. Pearson correlation coefficients between this seed signal, and BOLD signals from all other voxels were computed, resulting in a correlation map showing resting state connectivity between the seed and the rest of the brain.

All MEG data were filtered into frequency bands of interest (1-4Hz, 4-8Hz, 8-13Hz, 13-20Hz, 20-30Hz, 30-50-Hz, 50-70Hz). Data from the finger movement paradigm were processed using synthetic aperture magnetometry (SAM) in order to define a seed location. Resting state MEG data were projected from sensor space into source space using a beamformer spatial filtering technique. This yielded a single projected MEG timecourse for each voxel in a set of 5mm^3 voxels spaced uniformly across the brain. Each voxel timecourse was Hilbert transformed to compute the analytic signal; the absolute value of the analytic signal was derived giving the envelope of oscillatory power fluctuations within each frequency band. To compute connectivity, Pearson correlation coefficients between the Hilbert envelope at the seed location (in right sensorimotor cortex) and all other voxels were computed giving a correlation coefficient image for each frequency band, and for each subject.

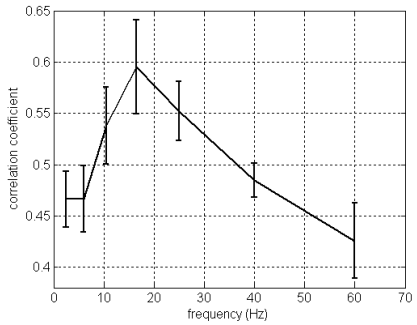

Figure 2: Correlation between fMRI and MEG functional connectivity images, plotted as a function of frequency. Results are averaged across all subjects and standard error is shown.

To obtain a quantitative estimate of the similarity between fMRI and MEG FC images, data from both modalities were co-registered to the subject's anatomical MR image. FC maps were smoothed using a 10mm FWHM Gaussian kernel to match the spatial resolution of the fMRI FC maps to the intrinsic spatial resolution of MEG. The correlation coefficient between the BOLD and MEG FC images for all 7 frequency bands were then computed and averaged across subjects.

Results: Figure 1 shows FC maps acquired using fMRI and MEG resting state data for a single representative subject. BOLD connectivity and MEG derived connectivity maps in the alpha (8-13Hz), low beta (13-20Hz) and high beta (20-30Hz) bands are shown, overlaid on the subjects own anatomical MRI. Although the superior spatial specificity of BOLD is apparent, there is also good spatial concordance between the fMRI and MEG FC images. Robust connectivity was observed in all subjects and an area in left sensorimotor cortex (average MNI coordinates of peak (-45±5, -31±6, 47±5)MEG and (-44±5, -29±9, 42±9)fMRI) showed high correlation with the seed in right motor cortex (average MNI coordinates of peak (46±7, -28±16, 50±6)MEG and (41±4, -16±7, 41±3)fMRI). Figure 2 shows the spatial correlation between the smoothed fMRI and MEG FC images, plotted as a function of MEG frequency band. Results are averaged across subjects and standard error is shown. Notice that the spatial concordance for the alpha and beta frequency bands is significantly higher than that in the delta, theta and gamma bands. The highest spatial correlation between fMRI and MEG occurred in the low beta band.

Discussion and Conclusion: In this study we have compared FC measured using fMRI and MEG. In fMRI, we exploit the high contrast to noise of 7T in order to obtain accurate FC images with high spatial specificity. In MEG we introduce a technique for connectivity measurement based on the correlation of the envelopes of band limited oscillatory power change. We have shown that connectivity in the sensorimotor network can be measured using both approaches and that the spatial signature of the network measured using MEG is in agreement with that measured using fMRI. Our finding that beta band fluctuations are heavily implicated in sensorimotor network connectivity is in strong agreement with our previous work, which has shown excellent spatio-temporal concordance between stimulus driven oscillatory power change in the beta band and the BOLD response. Our findings add weight to previous EEG/fMRI results that imply a neural oscillatory basis to the resting state BOLD response.

References: [1] Biswal et al.,(1995) MRM 34:537-541. [2] Birn et al., (2008) HBM 26:740-750. [3] Murphy et al., (2009) Neuroimage 44:893-905. [4] Laufs.(2008) HBM 29:762-769. [5] Stevenson et al. (2008) Proc. ISMRM, 2422.

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