Coupling between BOLD and electrophysiological brain network measurements

Joanne R Hale[1], Susan T Francis[1], Matthew J Brookes[1], and Peter G Morris[1]
[1]*SPMMRC, University of Nottingham, Nottingham, Nottinghamshire, United Kingdom*

Introduction: The study of functional brain networks is rapidly becoming an important area of neuroimaging[1]. Many recent studies have employed fMRI to delineate a set of orthogonal brain networks, some associated with simple sensory processing (visual, auditory, motor etc.) and others associated with higher-level processes (e.g., the dorsal attention network, default mode network (DMN) and salience network). These networks are key to healthy brain function and disruption within these networks has been implicated in various pathological conditions[2]. However, fMRI is limited since BOLD contrast is an in-direct measure of 'brain activity'. Electrophysiological techniques that facilitate a more direct measure of neuronal activity and allow measurement of interactions on a finer temporal scale are increasingly being used to provide complementary information. Here, we investigate network changes during an N-back working memory paradigm. We use parallel BOLD and magnetoencephalography (MEG) (a modality that measures magnetic fields induced directly by synchronised neural current flow) experiments to assess the relationship between haemodynamic and electrodynamic measures of network activity.

Methods: Eight subjects took part in both the fMRI and MEG experiments. *Paradigm*: Participants performed an N-back working memory task. Each trial comprised 4 phases of working memory: 0-back, 1-back, 2-back, 3-back and a rest period. During N-back phases, letters were presented sequentially every 2 seconds and subjects executed a button press when the current letter presented matched that shown *N* letters previously. Each phase lasted 33s; the order of the phases was randomised across trials. 10 trials were recorded in fMRI and 12 in MEG. During rest phases, a fixation cross was presented. In addition, in the MR session a 5 minute resting state BOLD fMRI acquisition was also performed. *fMRI acquisition:* BOLD data were acquired using a 7T Philips system. GE-EPI comprising 24 contiguous slices (TR/TE 1500/25ms, 1.5x1.5x3mm^3 resolution, 198x192 x72mm^3 FOV, SENSE factor 3) were acquired giving whole brain coverage. Homogeneous B_0 was achieved using a parcellated shimming procedure. *MEG acquisition:* MEG data were acquired using a 275 channel system (600Hz sample rate). Co-registration of MEG sensor locations to anatomical MRI was achieved using head digitisation (Polhemus Isotrack). *Data Analysis:* MEG data were filtered into frequency bands of interest and projected from sensor space to source space using a beamformer. For each voxel in source space, a Hilbert envelope was derived yielding a timecourse showing fluctuations in the envelope of oscillatory power for each frequency band. These envelopes were temporally smoothed (1s time resolution); concatenated across subjects; and analysed using temporal independent component analysis (ICA) yielding spatial maps corresponding to a set of electrodynamic brain networks[3]. The raw MEG data were then used to reconstruct time-frequency spectrograms showing changes in oscillatory power across the whole network. fMRI data were motion corrected, RETROICOR corrected[7] and spatially smoothed (4mm Gaussian kernel). For the resting state data, a seed-based correlation analysis (seed region in posterior cingulate cortex (PCC) for default mode network (DMN)) was carried out to form spatial maps of the DMN. N-back data were analysed with a GLM, generating statistical maps of brain regions exhibiting significant signal change time-locked to the task. This thresholded (FWE $p < 0.05$) statistical map was masked with the DMN map from the seed-based correlation analysis to ensure that a common DMN ROI was formed for use in subsequent analyses. The BOLD signal change with respect to rest across the DMN was then calculated for each of the N-back task phases.

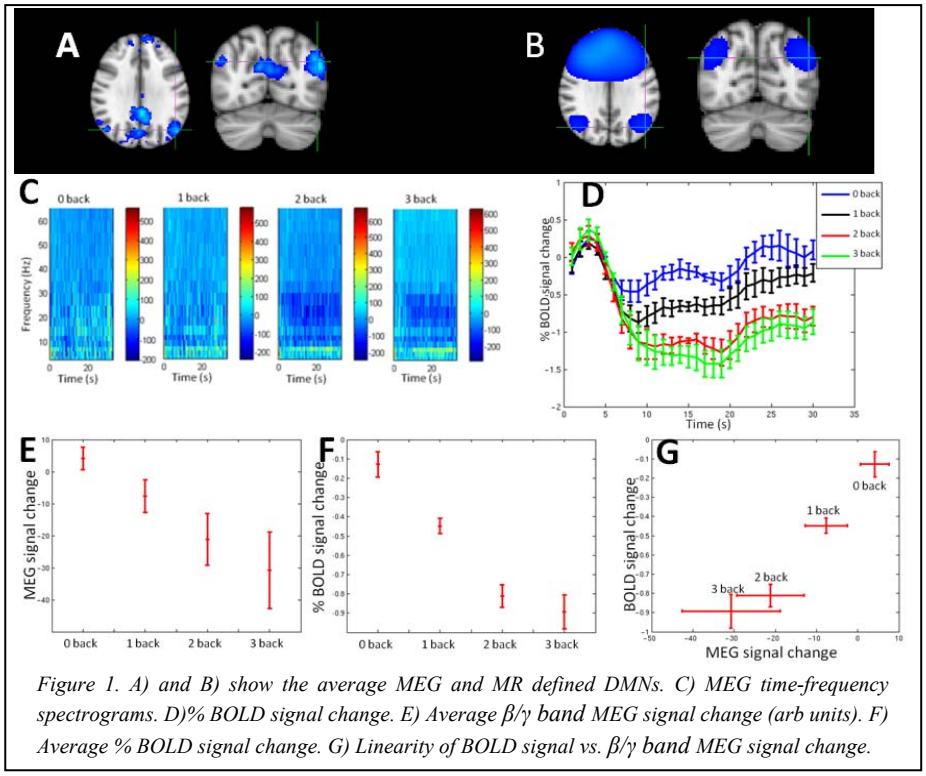

Figure 1. A) and B) show the average MEG and MR defined DMNs. C) MEG time-frequency spectrograms. D)% BOLD signal change. E) Average β/γ band MEG signal change (arb units). F) Average % BOLD signal change. G) Linearity of BOLD signal vs. β/γ band MEG signal change.

Results: Of a number of brain networks identified in both MEG and fMRI, here results focus on the DMN, which comprises medial frontal cortex, PCC and right/left lateral parietal cortices. Figure 1A shows the DMN identified using fMRI and Figure 1B shows its closest spatial match in MEG. Despite lower spatial resolution in MEG, three of the distinctive network nodes (medial frontal and left/right lateral parietal) are visible. Figure 1C shows the MEG time-frequency spectrogram, averaged across the DMN nodes for the 0-, 1-, 2-, and 3-back phases. Figure 1D shows the corresponding averaged BOLD timecourses. Note first that the mean BOLD amplitude reduction with task onset scales with increasing task difficulty (as indicated by *N*). In MEG, a similar scaling is observed with reductions in oscillatory power observed in the 13-40Hz range. However, note also that 13-40Hz power reductions are accompanied by concomitant increases in 4-8Hz (θ) oscillations. The mean change in oscillatory power (collapsed across the 13-70Hz band) for each phase is shown in Figure 1E, whilst Figure1F shows the equivalent % BOLD change, both showing power reductions scaling with N-back phase. Finally Figure 1G shows BOLD signal change plotted against 13-70Hz changes for each N-back phase, with a degree of non-linearity observed, possibly reflecting BOLD saturation at high *N*.

Discussion and Conclusions: DMN activity has previously been characterised by high temporal correlations measured between network nodes during the resting state, and a decrease in BOLD amplitude during tasks. Here, in agreement with previous work[5], we show that BOLD signal amplitude and MEG β/γ band power decreases in the DMN during an N-back working memory task compared with rest. Also in-line with previous work[6,7], we show that the magnitude of these signal changes scales with task difficulty (N). This work shows a close coupling exists between BOLD signals and neural oscillations, within functionally relevant networks. Further, the results shown here are in close agreement with invasive electrophysiological recordings[8]. The reduced spatial resolution associated with MEG is clearly apparent in the results shown. However, also apparent is the high time-frequency information content of MEG signals compared to BOLD. It therefore follows that a multi-modal approach to network measurements offers an excellent opportunity to study network behaviour with high spatial resolution and on a timescale relevant to brain function. As mentioned above, the DMN is only one of a number of networks identified as exhibiting spatial correlation across modalities. A multi-modal approach offers a promising way not only to understand functional connectivity between spatially distal network nodes, but also to probe interactions between networks.

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