Electrical and haemodynamic effects measured using MEG and combined EEG/fMRI

M. J. Brookes[1], K. J. Mullinger[1], C. M. Stevenson[1], G. B. Geirsdottir[1], R. W. Bowtell[1], and P. G. Morris[1]

[1]Sir Peter Mansfield Magnetic Resonance Centre, School of Physics and Astronomy, University of Nottingham, Nottingham, Nottinghamshire, United Kingdom

Introduction: Recent MEG studies [e.g. 1,2] have shown that characteristic neuronal responses can be measured in the ~100ms time window immediately following electrical stimulation of the median nerve. Such responses are usually characterized by their frequency distribution, and electrical power increases in the 1-40Hz and 50-200Hz frequency bands have been reported and shown to originate from primary motor and sensory cortices. In the present study, we aimed to measure these responses using both MEG, and EEG recorded simultaneously with functional MRI. Concurrent EEG/fMRI represents a powerful technique for exploration of the neuronal effects that underlie the BOLD response since it allows for simultaneous measurement of neuronal and haemodynamic effects. It is however made difficult due to the artifacts induced in the EEG data by the MR scanner. Recent advances [e.g. 3,4,5] have improved signal quality in concurrent measurements. Here, using averaged artifact subtraction and an EEG beamformer we show that evoked response and gamma band effects can be recorded using EEG/fMRI at 7T. Using equivalent beamformer analysis, we show that the EEG and MEG signals are spatially and temporally comparable. We also show that MEG and EEG effects are spatially coincident with the fMRI response.

Methods: Two subjects took part in the study which was approved by the local research ethics committee. The paradigm was equivalent for both EEG and MEG and involved electrical stimulation of the right median nerve at the wrist. A single trial comprised 8s of 2Hz stimulation followed by 8s rest. The experiment comprised a total of 30 trials with an experimental duration of 7mins30secs and a total of 480 median nerve stimuli.

<u>*MEG experiment:*</u> MEG data were recorded using the third order gradiometer configuration of a 275 channel CTF whole head MEG scanner at a sample rate of 600Hz. A 3D digitiser (*Polhemus Isotrack*) was used to record the shape of the subject's head for co-registration of MEG data to anatomical MRI data.

Source space analysis was undertaken using a MEG beamformer approach. Data were frequency filtered in the 1-40Hz (evoked) frequency band. Pseudo-T-statistical volumetric maps were then derived [6] showing the spatial distribution of stimulus related electrical power change. These images were overlaid onto anatomical images.

For timecourse analysis data were frequency filtered 1-40Hz (Evoked response) and 50–200Hz (gamma band). For both bands, beamformer estimated timecourses were extracted from a region of interest (ROI) derived from the Ŧ statistical map. The timecourse of evoked and gamma band activity at the ROI was averaged over all stimuli and plotted. Since MEG is insensitive to radial dipoles, the current orientation for the timecourse estimate was that producing maximum signal to noise ratio (SNR) in the tangential plane.

<u>*Concurrent EEG/fMRI experiment:*</u> EEG data were recorded using a *Brain Products* MR compatible 64 channel system with a sampling frequency of 5kHz. Echo planar images were acquired simultaneously using a 7T Philips Achieva scanner (TR = 2.2s; 96x96 matrix; TE = 25ms; in plane resolution = 2mm; 20slices; slice width 2mm.) The scanner and EEG clocks were synchronised for improved artifact correction [7]. Electrode locations were digitised using a 3D digitizer (*Polhemus Isotrack*).

Initial processing of EEG data was performed in *Brain Vision Analyzer* and involved gradient and pulse artifact correction using averaged artifact subtraction [3]. A vector beamformer was then applied [5] and Ŧ statistical images were constructed (equivalent to those created using MEG data). EEG data were frequency filtered 1-40Hz and 50–200Hz and for both bands, beamformer estimated timecourses were extracted from ROI's derived from the Ŧ statistical map. Timecourses of electrical activity, averaged across stimuli were plotted and compared to those derived using MEG. Since EEG is sensitive to radial dipoles, three separate time course estimates were made representing currents in the x, y, and z orientations. In order to estimate the total number of stimuli required to obtain a measurable gamma response, the SNR of the averaged response was plotted as a function of the number of stimuli averaged. The SNR was defined as the variance of the signal in the 10-50ms time window divided by the equivalent variance in the 400-440ms window. The number of stimuli used was varied between 1 and 461. For each value the SNR was calculated 100 times using different, randomly selected stimuli and results plotted with associated standard error. In order to allow for spatial comparison between EEG, MEG and fMRI results, the MR data were processed using SPM5.

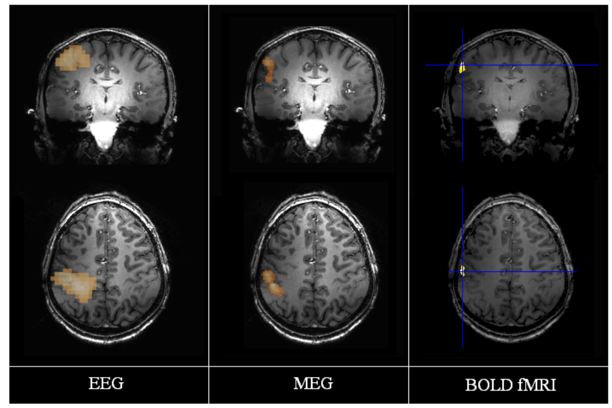

Fig. 1. Source localization using EEG, MEG and BOLD fMRI

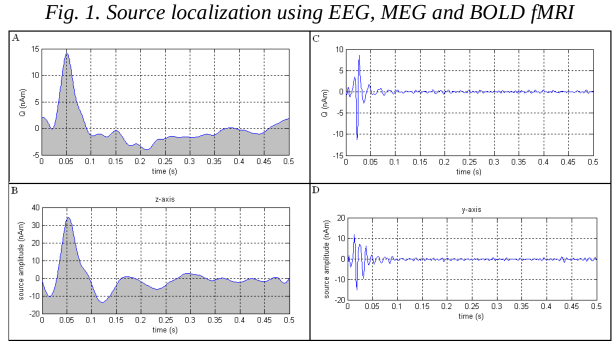

Fig. 2. Time courses of evoked and gamma effects from MEG & EEG

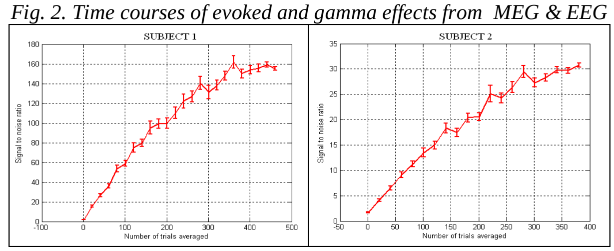

Fig. 3. Signal to noise ratios for the gamma band effect.

Results and discussion: Fig. 1 shows source localization of the evoked and BOLD responses in Subject 2. Localization of EEG (left), MEG (centre), and fMRI (right) effects are shown. Due to the conductivity profile across the brain, skull and scalp, EEG beamformer source localization is worse than the MEG equivalent. Despite this, the spatial agreement between the three modalities is compelling. Fig. 2 shows time course estimates of the MEG and EEG evoked and gamma band effects for Subject 1. Fig. 2A shows the MEG estimated evoked response; Fig. 2B shows the z-oriented EEG estimated evoked response; Fig. 2C shows the MEG estimated gamma response and Fig. 2D shows the y-oriented EEG estimated gamma response. In all cases timecourses are averaged over all stimuli. Note the agreement between EEG and MEG time course estimates even for the low amplitude gamma response. Fig. 3 shows the SNR for the gamma effect as a function of the number of trials averaged for both subjects. The overall SNR in Subject 2 was reduced due to increased head movement during the recording. As expected the SNR appears increases approximately with the square root of the number of averages. These data imply that a good signal to noise ratio can be recorded with approximately 20-30 averages.

Conclusion: We have shown that evoked responses and high frequency gamma band effects are measurable using concurrent EEG/fMRI at 7T. Further we show that the results obtained using EEG can be analysed in similar ways, and are comparable with, those recorded using MEG. Such MEG and concurrent EEG/fMRI measurements will be important for future studies investigating which of the measurable neuronal responses are most likely to underlie the fMRI BOLD response.

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