

Caffeine-induced Reductions in Motor Connectivity: A Comparison of fMRI and MEG Measures

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Introduction:

Resting state fluctuations in the blood oxygenation level-dependent (BOLD) signal have been used to identify temporally correlated functional networks [1-2], providing insights into brain architecture, communication pathways, and pathology. However, the interpretation of changes in BOLD connectivity can be complicated by the BOLD signal's complex dependence on changes in blood flow, volume, and metabolism. For example, caffeine (a neurostimulant and vasoconstrictor) has been shown to reduce BOLD connectivity and power in the motor cortex [3], but it is not known to what extent these reductions reflect caffeine's effect on neural connectivity and power as opposed to its effect on the neurovascular system. In this preliminary study, we used fMRI and magnetoencephalography (MEG) measures to determine the extent to which caffeine-induced changes in resting-state BOLD connectivity reflect underlying changes in neural connectivity.

Methods:

The study involved seven healthy individuals (aged 20-45) who were low caffeine users (<50 mg/day). Data were collected both prior to and 40 minutes after ingestion of a 200mg oral dose of caffeine or a placebo. Each subject participated in independent control and caffeine sessions with either MEG or fMRI acquisitions. **MEG:** Magnetic fields were recorded using an Elekta/Neuromag™ whole-head MEG system (VectorView) with 204 gradiometers and 102 magnetometers in a magnetically shielded room (IMEDCO-AG, Switzerland). Resting-state scans (5min length each) were conducted under the condition of eyes open with fixation. In addition, the subject was instructed to keep their mind blank and their hands in an open position. An additional empty-room dataset was collected as a reference for background noise levels. **fMRI:** BOLD data was acquired using a 3T GE MR750 system (EPI with 166 volumes, 30 slices, 3.438x3.438x5mm³ voxel size, 64x64 matrix size, TR=1.8s, TE=30ms). A 5-min resting-state functional scan (eyes open) was acquired in each session. In addition, high resolution anatomical data were collected using a magnetization prepared 3D fast spoiled gradient (FSPGR) sequence.

Data Analysis:

MEG: A temporal signal space separation based software (MaxFilter, Neuromag™) was used to remove artifacts due to magnetic interference from sources outside of the brain as well as head motion, eye blinks and movement, and cardiac activity. Next, a continuous wavelet transform (complex Morlet) was used to compute power time courses in different frequency bands (1 to 40 Hz in 1 Hz steps) [4]. For each band, the power was averaged over 500ms epochs followed by demeaning and detrending of the average power time courses. The correlations between the power time series from all pairs of sensors were then computed. **fMRI:** Nuisance regressors (0th+1st+2nd order Legendre polynomials, 6 motion time courses, and average BOLD signal from cerebral spinal fluid and white matter) were removed from the raw data through linear regression. The data were then low-pass filtered (0.08Hz). Each anatomical volume was registered using the functional data and warped to Talairach space. ROIs from the Brodmann atlas were then identified and warped back to the functional data space using an inverse affine transformation. An average BOLD signal was computed for each ROI and these were used to calculate the correlation values between all pairs of ROIs.

Results:

MEG: At rest, the majority of MEG signal power lies within the alpha band (8-12Hz). Thus, a Morlet wavelet centered at 10Hz was employed to obtain the power time courses used to form the correlation matrices. We focused on inter-hemispheric correlations between gradiometers located close (within 3.5cm) to the left and right primary motor and somatosensory cortices (corresponding to Brodmann areas 1-4). Across all subjects, caffeine-induced reductions in the mean inter-hemispheric gradiometer correlations (Fig. 1 – top row) were found to be statistically significant ($p = 0.03$) for the caffeine sessions, with no significant changes observed for the placebo sessions ($p = 0.5$). Changes in mean MEG power (averaged across channels and time) were not found to be significant ($p = 0.82$) for the caffeine sessions.

fMRI: Across all subjects, caffeine-induced reductions in inter-hemispheric BOLD connectivity (Fig. 1 – bottom row; correlation averaged across Brodmann areas 1-4) were determined to be statistically significant ($p = 0.05$) in the caffeine session but not significant for the placebo sessions ($p = 0.39$). In Figure 2, the difference between the post-dose and pre-dose correlation coefficients from the caffeine sessions is plotted for each subject for both modalities. No significant correlation was found between the amplitude of the changes ($p = 0.27$). However, the sign of the change appears to be consistent across modalities. As a test of this consistency, we found that the pairwise product of the correlation changes (which is positive if the signs are the same) was significantly greater than zero ($p= 0.03$).

Discussion:

Our preliminary findings suggest that caffeine-related decreases in BOLD correlation reflect a decrease in neural connectivity, as measured with MEG. While the sign of the change in connectivity measures is consistent between fMRI and MEG, the actual amplitudes of the changes are not significantly correlated. Thus, it is likely that non-neural factors (e.g. vascular changes) are also influencing the observed changes in fMRI connectivity. In this work, we computed MEG connectivity at the sensor level. Future work with source-based analysis will be useful for further elucidating the relation between MEG and fMRI connectivity measures.

References: [1] Biswal, B. et al, Magn. Reson. Med., 34:537-541, 1995. [2] Fox, M.D et al, J. Neurophysiol 101:3270-3283, 2009. [3] Rack-Gomer, A.L. et al, NeuroImage 46(1):56-63, 2009. [4] Tallon-Baudry, C. et al, J. Neurosci., 17(2):722-34, 1997.

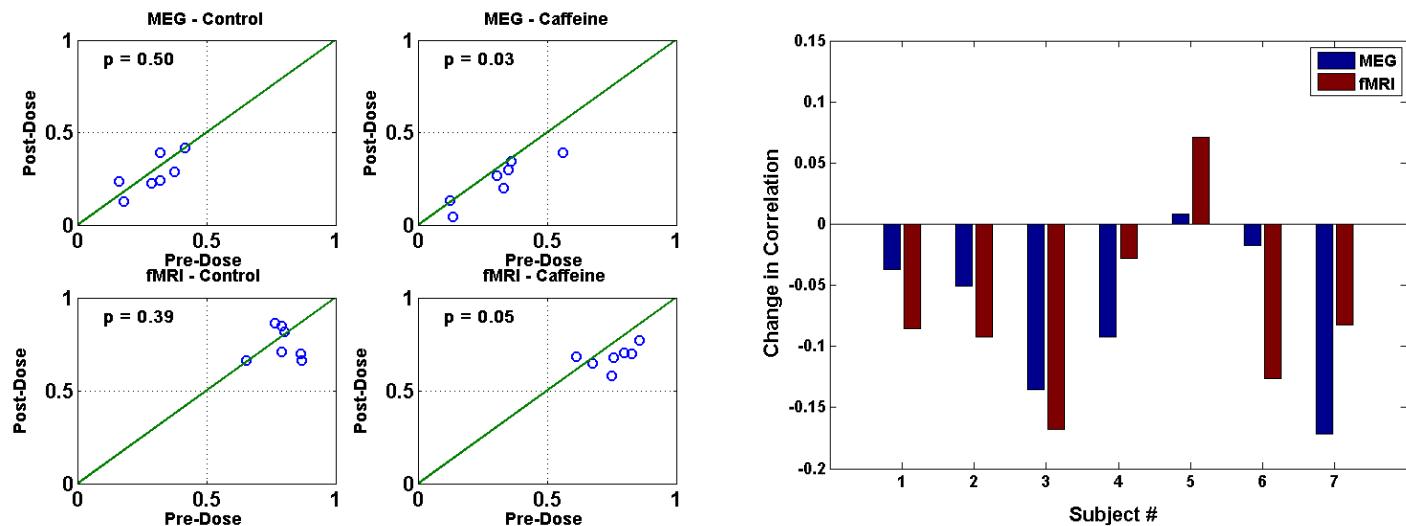


Figure 1: Post-dose vs. pre-dose correlation values for control (left) and caffeine sessions (right) with MEG and fMRI measures shown in top and bottom rows, respectively.

Figure 2: Difference between post-dose and pre-dose correlation values for MEG (blue) and fMRI (red).