

# Identification of whole brain correlation patterns between resting-state fMRI signal amplitude and EEG vigilance in eyes-closed and eyes-open conditions

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## PURPOSE

In resting-state functional MRI, pre-processing of the BOLD data often includes a controversial step known as global signal regression, which may produce spurious anti-correlation<sup>1,2,3</sup>. Using simultaneous EEG-fMRI, a recent study found that the amplitude of the global signal is negatively correlated (across subjects and runs) with a measure of EEG vigilance in the eyes-closed condition but not in the eyes-open condition<sup>4</sup>. In this study, we examined the spatial distribution of the correlations between the BOLD signal and EEG vigilance and compared these across eyes-closed and eyes-open conditions. We found that the amplitudes of the BOLD signal (as measured across subjects and runs) in the motor cortex, middle temporal gyrus, basal ganglia, and cuneus are significantly more negatively correlated with EEG vigilance measures in the eyes-closed condition as compared with the eyes-open condition.

## METHOD

Simultaneous EEG-fMRI data were acquired on ten healthy subjects (4 males and 6 females) during three eyes-closed (EC) and three eyes-open (EO) resting-state runs (from three separate scan sessions; one EC and one EO run in each session) using a 3 Tesla GE MR750 system and a 64 channel EEG system (Brain Products). EEG signals were recorded at a 5kHz sampling rate and MR gradient artifacts were removed using Vision Analyzer 2.0 software (Brain Products). The resulting signals were low pass filtered (fc = 30Hz) and then down-sampled to 250Hz. To remove cardio-ballistic and residual artifacts, OBS-ICA was applied as implemented in EEGLAB<sup>5,6</sup>. A spectrogram was created using a short-time Fourier transform with a 1311 point 4-term Blackman-Harris window and 65.7% overlap, resulting in 1.8s temporal resolution. Functional MRI data were acquired with the following parameters: echo planar imaging with 166 volumes, 30 slices, 3.4x3.4x5mm<sup>3</sup> voxel size, 64x64 matrix size, TR=1.8s, TE=30ms. Nuisance regressors (1<sup>st</sup>+2<sup>nd</sup> order Legendre, 6 motion time courses and their first derivatives, mean BOLD signals from the WM and CSF voxels and their first derivatives, RETROICOR<sup>7</sup> and RVHRCOR<sup>8</sup> noise terms) were removed from the raw data through linear regression. Outlier detection was applied to the mean of all EEG amplitude time courses to remove motion-contaminated time segments from both the spectrogram and fMRI time series.

For each time point and channel in the spectrogram matrix, the value in each frequency bin was divided by the root mean square (rms) of the bin values across frequencies. A relative EEG amplitude spectrum was then calculated by taking the rms of the normalized spectrogram entries across time and channels. Relative EEG amplitudes were derived from the relative amplitude spectrum as the rms of the frequency bin values across different frequency bands (delta: 1-4Hz, theta: 4-7Hz, alpha: 7-13Hz, beta: 13-30Hz). A measure of vigilance was then defined as the relative alpha amplitude divided by the rms of the relative delta and theta amplitudes<sup>4</sup>. For each voxel, a percent change BOLD time series was obtained by subtracting the mean value and then dividing the resulting difference by the mean value. The BOLD amplitude was formed by calculating the standard deviation of the percent change time series. The EEG vigilance was then correlated with the BOLD amplitude across subjects and scans on a per voxel basis. In addition, the correlation values were converted to z-scores using the Fisher z-transformation and then the z-score amplitude obtained in the eyes-open condition was subtracted from the eyes-closed condition. Statistical significance of the difference was assessed using a permutation test<sup>9</sup>.

## RESULTS AND DISCUSSION

The first and second rows of Fig. 1 displays the whole brain voxel-wise correlation between EEG vigilance and BOLD amplitude across subjects and scans in the eyes-closed (EC) and eyes-open (EO) conditions, respectively (corrected, p<0.05). We observed more widespread negative correlations in the eyes-closed condition as compared with the eyes-open condition. To quantify the correlation difference, the third row of Fig. 1 shows the difference of the z-scores (corrected, p<0.05). We observed significant differences in the motor cortex, middle temporal gyrus, basal ganglia, and cuneus -- brain regions that have previously been found to be associated with various aspects of vigilance<sup>10,11</sup>. The current findings suggest that these regions may also be responsible for the stronger association between EEG vigilance and the BOLD global signal that is observed in the eyes-closed condition.

[1] Fox et. al., PNAS 2005, 102: 9673-9678. [2] Fox et. al., J Neurophysiol 2009, 101:3270-3283. [3] Murphy et. al., Neuroimage 2009, 44:893-905. [4] Wong et. al., Neuroimage 2013, 83:983-90. [5] Delorme et. al., J of Neuroscience Methods 2004, 134:9-21. [6] Debener et. al., Neuroimage 2007, 34:587-597. [7] Glover et. al., Magn Reson Med 2000, 44:162-167. [8] Chang et. al., Neuroimage 2009, 47:1448-1459. [9] Bullmore et. al., IEEE Trans. Med. Imaging 1999, 18:32-42. [10] Breckel et. al., Neuroimage 2011, 1754-62. [11] Drummond et. al., Sleep 2005, 1059-68.

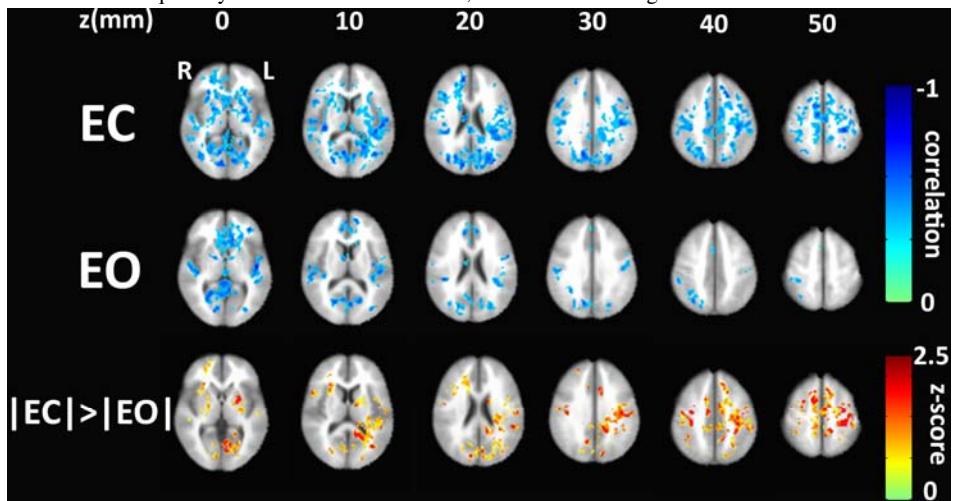


Fig. 1 Top 2 rows: Correlation between EEG vigilance and BOLD amplitude across subjects and runs on a per voxel basis (p<0.05, corrected). Third row: Difference in correlation amplitude (Fisher z-transformed), statistical significance assessed using permutation test (p<0.05, corrected).