Inter-subject variability in the amplitude of the resting-state fMRI global signal reflects differences in EEG vigilance

Chi Wah Wong[1], Valur Olafsson[1], Omer Tal[1], and Thomas Liu[1]
[1]*Center for Functional MRI, University of California San Diego, La Jolla, CA, United States*

PURPOSE

In resting-state functional MRI, global signal regression is often applied to remove physiological noise from the BOLD time courses [1, 2, 3]. Although many studies treat the global signal as a non-neural confound, a recent study using electrophysiological and fMRI measures in primates has shown that the global signal contains significant neural contributions [4]. Using simultaneous EEG-fMRI, we performed an inter-subject variability analysis to examine the neuro-electrical basis of the global signal in humans. We show that the global signal amplitude is negatively correlated with an EEG-based vigilance measure.

METHOD

Simultaneous EEG-fMRI data were acquired on ten healthy subjects (4 males and 6 females) during three 5-minute eyes-closed resting-state runs (from 3 separate scan sessions) using a 3 Tesla GE MR750 system and a 64 channel EEG system (Brain Products). EEG signals were recorded at 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 [5, 6]. For each channel, a spectrogram was created using a short-time Fourier transform with 1311 point 4-term Blackman-Harris window and 65.7% overlap. Functional MRI data were acquired with the following parameters: echo planar imaging with 166 volumes, 30 slices, 3.438x3.438x5mm^3 voxel size, 64x64 matrix size, TR=1.8s, TE=30ms. Nuisance regressors (0th+1st+2nd order Legendre, 6 motion time courses and their first derivatives, mean BOLD signals from the WM and CSF voxels and their first derivatives, RETROICOR [7] and RVHRCOR [8] noise terms) were removed from the raw data through linear regression. Outlier detection was applied to the mean (across channels) of the EEG amplitude time courses in order to identify and remove motion-contaminated time segments from both the spectrograms and fMRI time series.

For each time point and channel in the spectrogram, a relative amplitude spectrum was computed by normalizing the spectrum by its overall power. These spectra were then averaged (root mean square (rms)) across time points and channels to generate a mean spectrum for each scan. Relative EEG amplitudes were computed as the rms amplitude in the following frequency bands (delta: 1-4Hz, theta: 4-7Hz, alpha: 7-13Hz, beta: 13-30Hz). A measure of vigilance was defined as the rms amplitude in the alpha band divided by the rms amplitude in the delta and theta bands [9]. 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 global signal amplitude was formed by averaging the percent change time series across all brain voxels and then calculating the standard deviation.

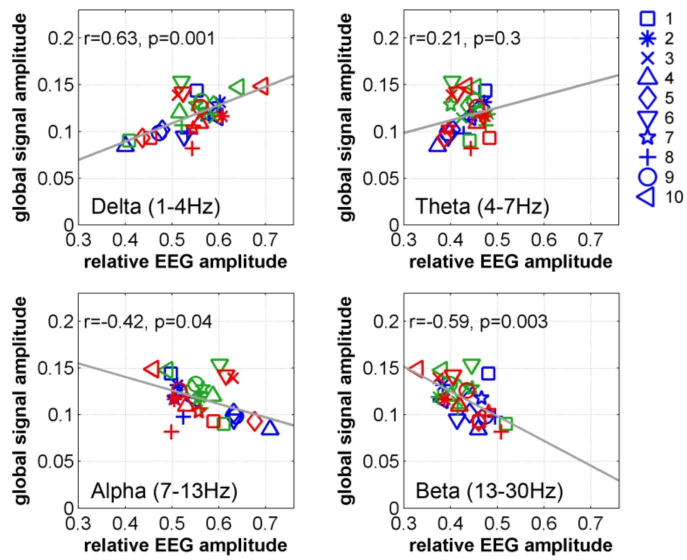

Fig. 1 Global signal amplitude and relative EEG amplitude at different frequency bands. Different colors for each symbol indicate different scan session for the same subject.

RESULTS AND DISCUSSION

Fig. 1 displays the global signal amplitude versus the relative EEG amplitudes in the different frequency bands. We found a significant positive correlation in the delta band and negative correlation in the alpha and beta bands. These relations suggest that there may be a change in the shape of the EEG spectra across different global signal amplitude levels. Fig. 2 shows the relative amplitude EEG spectra for three representative runs with different levels of global signal amplitude. Spectra corresponding to smaller global signal amplitudes (e.g. red curve) exhibit lower relative delta (1-4Hz) and higher relative alpha (7-13Hz) and beta (13-30Hz) amplitudes. The spectra with lower relative delta and higher alpha power are associated with a higher level of vigilance. Fig. 3 shows a significant negative correlation (r = -0.45) between the global signal amplitude and EEG vigilance measure. In summary, the amplitude of the resting-state global signal reflects the vigilance state of the subjects, with greater vigilance levels corresponding to lower global signal amplitudes. Our findings suggest that removing the global signal during pre-processing may minimize the variability in fMRI connectivity measures that is due to differences in vigilance across subjects.

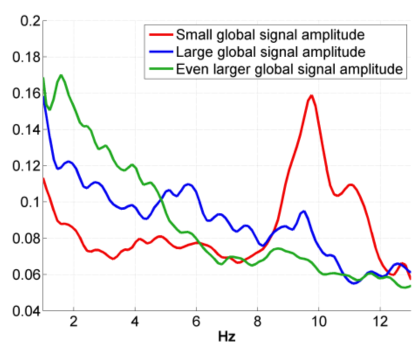

Fig. 2 EEG relative amplitude spectra for three representative runs

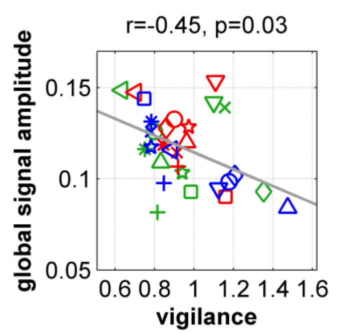

Fig. 3 The global signal amplitude and vigilance measure

[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]** Scholvinck et. al., PNAS 2010, 107:10238-10243. **[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]** Olbrich et. al., Neuroimage 2009, 45:319-332.