Differences in the resting-state fMRI global signal amplitude between the eyes open and eyes closed states are related to changes in EEG vigilance

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PURPOSE

In resting-state functional MRI, pre-processing of the BOLD data often includes the removal of the global signal[1,2,3]. Using simultaneous EEG-fMRI, a recent study found that the amplitude of the global signal is negatively correlated with a measure of EEG vigilance in the eyes-closed condition[4]. In this study, we assessed the relation between global signal amplitude and EEG vigilance values in the eyes open (EO) and eyes closed (EC) resting states. In particular, we examined the relation between changes (EO minus EC) in the global signal amplitude and associated changes in EEG vigilance, and compared this relation to the previously reported finding of a negative correlation between the caffeine-induced changes in global signal amplitude and EEG vigilance[4].

METHODS

Simultaneous EEG-fMRI data were acquired on ten healthy subjects (4 males and 6 females) during two eyes-closed (EC) and two eyes-open (EO) resting-state runs (from two 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 [5,6]. 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^3 voxel size, 64x64 matrix size, TR=1.8s, TE=30ms. Nuisance regressors (1st+2nd order Legendre, 6 motion time courses and their first derivatives, mean BOLD signals from white matter 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 of all EEG amplitude time courses to remove motion-contaminated time segments from both the spectrogram and fMRI time series.

For each voxel, a percent change time series was obtained from the pre-processed BOLD time series by subtracting the mean value and then dividing the resulting difference by the mean value. A global mean signal was formed as the average of the percent change time series across all voxels within the brain, and the global signal amplitude was defined as the standard deviation of this mean signal.

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[4]. For each subject, the global signal amplitude and EEG vigilance measures were averaged across the two scan sessions.

RESULTS AND DISCUSSION

As shown in the Fig. 1a, there was a significant negative correlation (r=-0.79, p=0.007) between the changes (EO-EC) in global signal amplitude and EEG vigilance. Consistent with the negative values of the EO-EC changes shown in Fig. 1a, there was a significance decrease in global signal amplitude with opening of the eyes (t(9)=-3.1, p = 0.01). The amplitude spectra from two representative subjects are shown in Figs. 1b and 1c. The amplitude spectra were calculated by averaging the global relative amplitude spectra across the two scan sessions. In Fig. 1b, there is relatively little change in the spectra between the EC and EO conditions, corresponding to a relatively small change in both the global signal amplitude and vigilance. In contrast, the spectra in Fig 1c shows a pronounced shift towards higher frequencies in the EO condition as compared to EC, corresponding to a large increase in vigilance and a large decrease in the global signal amplitude. In Figure 2, the differences (EO-EC) in global signal amplitude versus differences in vigilance from Figure 1a are plotted in blue, while the caffeine-related changes (post-dose minus pre-dose) in these metrics that were previously reported in ref. 4 are plotted in red. The blue and red lines indicate the linear fits to the EO-EC and caffeine data, respectively. There was not a significant difference (F(1,16)=0.45, p=0.51) in the slopes of the blue and red lines. The gray line indicates the overall linear fit to all of the data, which showed a significant negative correlation between changes in global signal amplitude and vigilance (r=-0.91, p=0.0002). Our findings provide further support for the existence of a fundamental relationship between global signal amplitude and EEG vigilance. Furthermore, they suggest that previously reported differences in functional connectivity between the EO and EC states may largely reflect differences in vigilance levels[9].

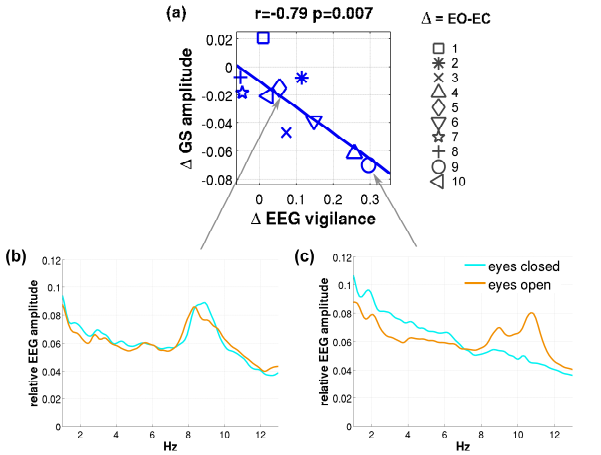

Fig. 1 (a) The change (EO-EC) in the average global signal amplitude is negatively correlated with the change in average EEG vigilance. (b,c) EEG spectra for two representative subjects (indicated by the diamond and circle symbols in panel a. Spectra from the EO and EC states are shown by the cyan and brown lines, respectively.

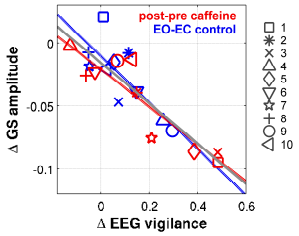

Fig. 2. Changes (EO-EC) in the average global signal amplitude versus associated differences in EEG vigilance are indicated by the blue symbols with the linear fit shown by the blue line. Changes (post-dose caffeine minus pre-dose) in the global signal amplitude versus the associated changes in EEG vigilance from ref. 4 are indicated by the red symbols with the linear fit shown by the red line. There was not a significant difference in the slopes of the red and blue lines. The solid grey line shows the overall linear fit to all the data points.

[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]** Jao et al, Neuroimage 2013. 69:21-34.