Temporal variations in the resting-state fMRI global signal amplitude are correlated with time-varying measures of network topology parameters and EEG vigilance

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PURPOSE

Global signal regression, albeit controversial, is commonly applied to remove physiological noise from the BOLD time courses in resting-state functional MRI studies [1,2,3]. A recent simultaneous EEG/fMRI study has shown that the amplitude of the global signal is negatively correlated with a measure of EEG vigilance across subjects and runs [4]. The metrics used in the previous study were calculated over the entire run (5 minutes). In this study, we adopted a sliding window approach and examined how the temporal dynamics of the global signal amplitude are related to the dynamics of whole brain functional connectivity and EEG vigilance. We found that the temporal variations in global signal amplitude are 1) positively correlated with the time-varying clustering coefficient, and 2) negatively correlated with time-varying measures of both the characteristic path length and EEG vigilance.

METHOD

Simultaneous EEG-fMRI data were acquired on ten healthy subjects (4 males and 6 females) during three 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 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. For each session, high resolution anatomical data were acquired using a magnetization prepared 3D fast spoiled gradient (FSPGR) sequence. Each anatomical volume was registered with the functional data and then segmented into cortical regions using Freesurfer parcellation [7]. Nuisance regressors (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 [8] and RVHRCOR [9] 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 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). At each time point, 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 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 was formed by averaging the percent change time series across all brain voxels.

To assess temporal variations in the global signal amplitude, functional connectivity and EEG vigilance, we applied a sliding window (30s) over the length of each run. Within each window, the amplitude of the global signal was obtained by taking the standard deviation. In addition, the root mean square of the EEG vigilance (rms vigilance) was calculated. To calculate whole brain connectivity, we obtained an averaged time course for each ROI in the cerebral cortex (as identified using Freesurfer) and then correlated the time courses across all ROI pairs (2628 pairs). Network analysis was then applied to the whole brain connectivity matrix using the Brain Connectivity Toolbox (BCT) [10]. Characteristic path length and clustering coefficient were then retrieved to describe the level of integration and segregation, respectively.

RESULTS AND DISCUSSION

Fig. 1 plots the temporal variations of the global signal amplitude along with the characteristic path length, clustering coefficient, and rms vigilance over the length of one run extracted from a representative subject (the time courses were normalized to zero mean and unit variance). For display purposes, the characteristic path length and rms vigilance are multiplied by -1. We found that the global signal amplitude is positively correlated with the clustering coefficient and negatively correlated with the characteristic path length, suggesting that dynamic increases in global signal amplitude are associated with increasing network integration and clustering. In addition, temporal variations of the global signal amplitude are negatively correlated with variations in rms vigilance. Fig. 2 displays the mean and standard deviation of temporal correlations between the global signal amplitude and network metrics across subjects and runs, with correlations significantly different from zero across the sample (t-test, p<0.001, corrected). The temporal correlations between the global signal amplitude and rms vigilance were also significantly different from zero (mean=-0.11, p=0.03). Our findings suggest that global signal regression may reduce the temporal variations of resting-state brain topology measures associated with dynamic changes in alertness.

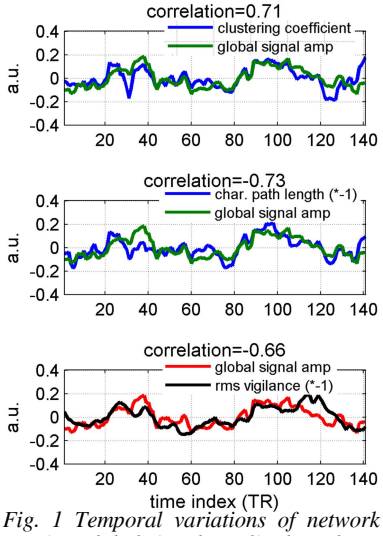

Fig. 1 Temporal variations of network metrics, global signal amplitude and rms vigilance. The rms vigilance and characteristic path length curves are multiplied by -1.

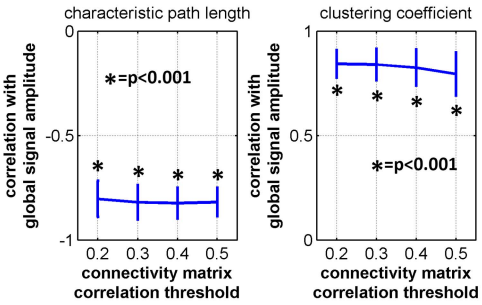

Fig. 2 Temporal correlation between network metrics and the global signal amplitude (mean/s.d. across subjects and runs)

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