The Amplitude of the Resting State fMRI Global Signal Is Related to EEG Vigilance Measures

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BACKGROUND

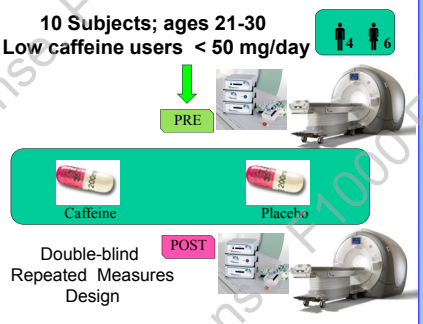
In resting-state functional MRI, global signal regression is often applied to remove physiological noise from the BOLD time courses [1, 2]. Although many studies treat the global signal as a non-neural confound, a recent study using electrophysiological and fMRI measures in primates has shown that the global signal contains significant neural contributions [3]. In this study, we used simultaneously electroencephalographic (EEG) and fMRI measures of resting-state activity to assess the relation between the global signal amplitude and EEG measures of vigilance in humans. The major findings are:

- **The amplitude of the global signal exhibited a significant negative correlation with EEG vigilance across subjects and runs**
- **The caffeine-induced change in the amplitude of the global signal exhibited a significant negative correlation with the associated change in EEG vigilance across subjects**

METHODS

5-minute resting-state runs (one for each pre/post dose, caffeine/placebo sessions) with eyes-closed. 64 channel EEG data were recorded (Brain Products). Functional MRI data were acquired using a 3T GE MR750 system with the following scan parameters: echo planar imaging with 166 volumes, 30 slices, 3.438x3.438x5mm^3 voxel size, 64x64 matrix size, TR=1.8s, and TE=30ms.

10 Subjects; ages 21-30
Low caffeine users < 50 mg/day



Double-blind
Repeated Measures
Design

fMRI data processing

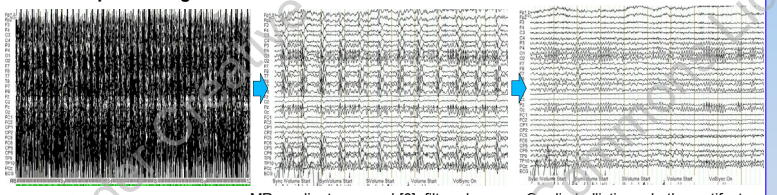
RAW BOLD time series → Corrected BOLD time series → %ΔBOLD time series

Nuisance covariates:
- Legendre
- RETROICOR [4]
- RVHRCOR [5]
- Motion time courses
- CSF
- White matter

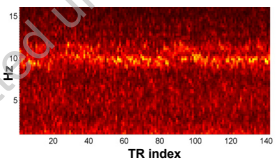
$= [\beta_1 \beta_2 \ldots \beta_n] +$

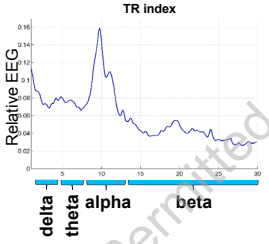
Global signal = mean of all %Δ BOLD time courses in the brain
Global signal amplitude = root mean square (rms) of the global signal

EEG data processing



Original data | MR gradient removed [6], filtered (fc=30Hz), and down-sampled to 250Hz | Cardio-ballistic and other artifacts removed [7,8,9]





Spectrograms were created using a short-time Fourier transform with 4-term Blackman-Harris window (1311 points, 5.24 s temporal width, and 65.7% overlap). Relative amplitude spectra were computed by normalizing each spectrum by the square root of the the sum of squares across frequency bins. A global relative amplitude spectrum was created by taking the rms of the relative spectra across time points and channels.

Relative EEG amplitudes were then computed as the rms amplitude in the following frequency bands (delta: 1-4 Hz, theta: 4-7 Hz, alpha: 7-13 Hz, beta: 13-30 Hz).

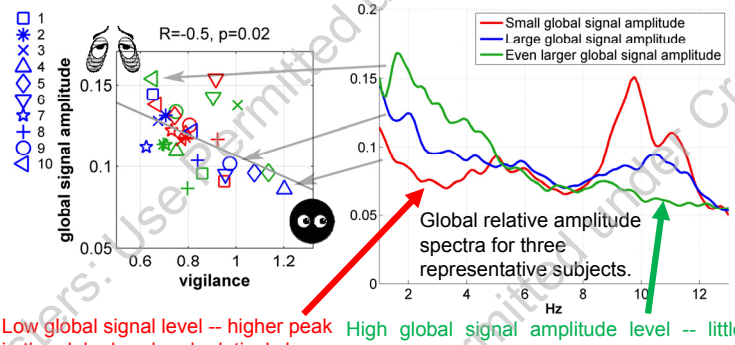
A measure of vigilance was defined as the rms amplitude in the alpha band divided by the rms amplitude in the delta and theta bands [10].

$$\text{EEG vigilance} = \frac{\text{Alpha}}{\text{Delta and Theta}}$$

RESULTS

Caffeine session pre-dose (blue), control session pre-dose (red) /post-dose sections (green)

Fig. 1



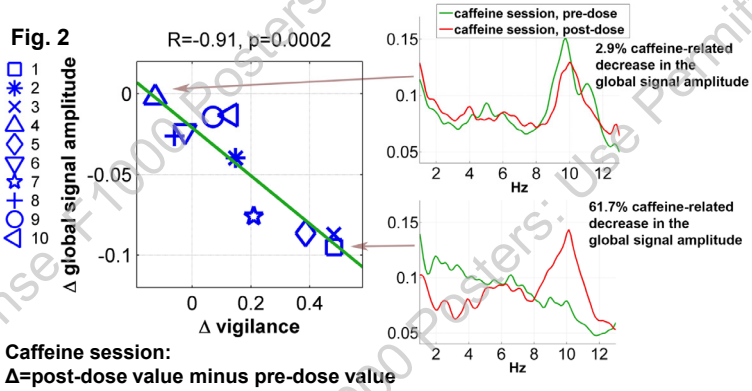
Global relative amplitude spectra for three representative subjects.

Low global signal level -- higher peak in the alpha band and relatively low power in the delta band.

High global signal amplitude level -- little power in the alpha band and much greater power in the delta band.

The left panel of Figure 1 displays the global signal amplitude versus the EEG vigilance measure (with motion amplitudes and heart rate covariates projected out prior to display). A significant negative correlation (R=-0.5, p=0.02) was found, with an increase in vigilance corresponding to a reduction in the global signal amplitude.

Fig. 2



Caffeine session:
Δ=post-dose value minus pre-dose value

The left panel of Figure 2 displays the caffeine-related change in the global signal amplitude versus the associated change EEG vigilance measure. A significant negative correlation (R=-0.91, p=0.0002) was found, with a larger caffeine-induced increase in vigilance corresponding to a larger reduction in the global signal amplitude.

DISCUSSION

- 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 and runs.

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