

# CORRELATED SLOW FLUCTUATIONS IN RESPIRATION, EEG, AND BOLD FMRI: WHAT IS THE ORIGIN OF PHYSIOLOGICAL NOISE?

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**INTRODUCTION:** It has been widely observed and reported that physiological activity, such as cardiac and respiratory activity, affects BOLD fMRI [1,2]. These physiological activities are considered of marginal interest to the underlying neural activity and thus are removed from fMRI data, especially when studying the spontaneous fluctuations at resting state. The corrected physiological noise includes effects related to the respiratory and cardiac cycles as well as the slow fluctuation in the rate of respiratory volume and heart beats [3,4]. While the slow temporal fluctuation (<0.1 Hz) in respiratory volume has been presumably considered as a source of physiological noise, its possible neurological origin, however, has not been investigated. In this study, we recorded, simultaneously with BOLD fMRI, electroencephalography (EEG) as a direct measure of electric brain activity alongside subjects' respiration waveforms at resting state in order to investigate and to unravel for the first time the relationship between the slow fluctuations in band-limited EEG power, respiration, and BOLD signals.

**METHODS:** Nine healthy human subjects (age  $33 \pm 10$  years; one female) participated in the study. The experiments were performed on a General Electric Discovery MR750 3T MRI scanner with an 8-channel receive-only head array coil. For the whole brain fMRI, a single shot gradient echo EPI sequence with Sensitivity Encoding (SENSE) and FOV/slice thickness=220/2.9mm was used ( $TR/TE=2000/30$ ms, acceleration=2, image matrix=128 $\times$ 128, flip=30° [5], and 34 axial slices). High-density EEG signals from 126 channels were simultaneously recorded with BOLD fMRI scans using MRI-compatible BrainAmp MR Plus amplifiers (in 0.016–250 Hz band with 0.1  $\mu$ V resolution and 5000 Hz sampling rate). Subjects were asked to rest with their eyes closed or open (looking at a fixation cross). The closed-eye and open-eye sessions were repeated twice for each subject, and each session lasted for six minutes and ten seconds. A pneumatic respiration belt and a photoplethysmograph were used for respiration waveform and pulse oximetry measurements, respectively. Using similar configurations, concurrent EEG and respiration waveform data were recorded separately (on different days) in three of the nine subjects in a mock MRI scanner, which provided a dark and quiet non-magnetic environment resembling the visuospatial aspects of MRI.

Respiration volume per time (RVT) was derived using the method described by Birn et al. [4]. After correcting the gradient and ballistocardiac artifacts in EEG recorded inside scanner, the band-limited power in alpha frequency band (8–13 Hz) was extracted and averaged across all electrodes, i.e. global field power (GFP). Cross correlation was assessed between the time courses of RVT and alpha GFP over lags from -100 s to 100 s. The correlation coefficient was calculated at the lag with maximum cross correlation. To evaluate their effect on BOLD signals, the time courses of RVT and EEG were shifted with delays of (0, 1, ..., 9)  $\times$  TR and the voxel-wise correlation between the shifted RVT/EEG and BOLD was calculated.

**RESULTS:** As shown in Fig. 1A-F, significant correlation between RVT and EEG alpha band GFP was observed in the closed-eye condition, in contrast to the much less correlation in the open-eye condition. Maximum correlation coefficient ( $CC = 0.29 \pm 0.08$ , averaged across subjects) was obtained when GFP lead RVT by 3.28 s for closed-eye condition, which is significantly different from that in open-eye condition ( $CC = 0.11 \pm 0.07$ ). Similar correlation between RVT and alpha band GFP was observed in recordings acquired inside scanner as well as outside of scanner, as shown in Fig. 1A&C (data from a representative subject). In the same subject, CC between BOLD and time-shifted EEG alpha band GFP or RVT is shown in Fig 1.G & H. The plotted CC between BOLD and GFP was obtained by shifting GFP 3 $\times$ TR, which corresponds to the peak time (6 s) of a canonical hemodynamic response function. Such image appear very similar to the CC between BOLD and RVT shifted by 1 $\times$ TR (considering RVT lag GFP by approximately 2 $\times$ TR).

**DISCUSSION:** Our results have demonstrated for the first time significant correlation between alpha-band EEG power, respiration, and spontaneous fluctuations of BOLD signal at resting state. In particular, the EEG-respiration correlation during closed-eye resting is significantly stronger than that during open-eye resting. Since the alpha-power variation reflects the fluctuation of consciousness level, the correlation between alpha EEG and respiration indicate they may be commonly affected by the consciousness at rest. Our finding suggests that respiration fluctuations reflect and are linked to the underlying brain electrophysiological activity.

Many studies investigating the electrophysiological correlates for BOLD resting state networks (RSNs) have considered the band-limited EEG power, such as in the alpha band [6,7]. Since respiration is tightly related to the cerebral level of  $CO_2$  and thus directly affects the BOLD signal, the correlation between alpha EEG, respiration, and BOLD may commonly originate from the fluctuation of consciousness level, which may override the signal associated with the RSNs. Considering the EEG-respiration-BOLD correlation, alpha-band EEG power may not be optimal and desirable for studying the electrophysiological correlates for BOLD RSNs.

**REFERENCES:** [1]Kruger G. et al. MRM **46**,631,2001; [2]Bodurka J. et al. Neuroimage **34**,542,2007; [3]Shmueli K. et al. Neuroimage **38**,306,2008; [4]Birn R. et al. NeuroImage **31**,1536, 2006; [5]Gonzalez-Castillo J. et al. Neuroimage **54**,2764,2011; [6]Goldman R.I. et al. Neuroreport **13**,2487,2002; [7]Laufs H. et al. Proc. Natl. Acad. Sci. **100**,11053, 2003.

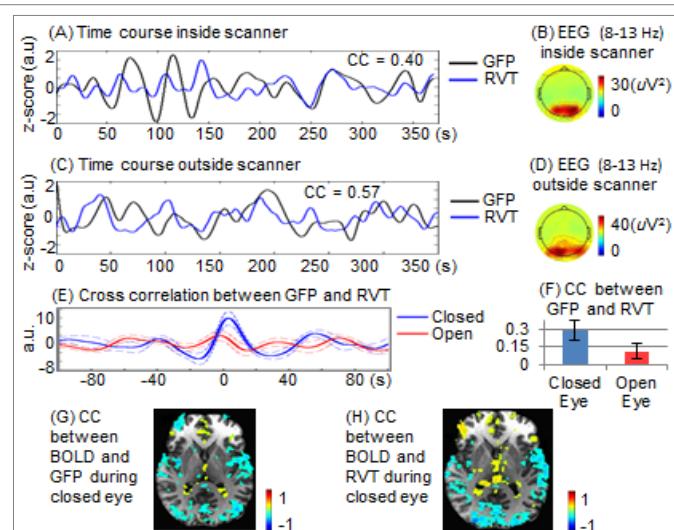


Fig. 1 Correlation between EEG alpha-band GFP, RVT and BOLD