Correction of the Low-Frequency Physiological Noise in the Resting State BOLD fMRI - Effect on the ICA Default-Mode Analysis at 1.5T

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Introduction:

In the studies of low-frequency resting state networks (RSN) the impact of aliased physiologic noise has been a persistent source of criticism and uncertainty in the interpretation of the results. More recently, lagged estimates of the low-frequency physiological noise fluctuations (respiratory (1) and cardiac (2)) have been shown to explain notable signal variance in the regression analysis of the RSNs, affecting particularly the so called default mode network (DMN). DMN spatially overlaps with regions significantly affected by physiologic low-frequency fluctuations and they occur at similar frequencies. Exact physiological mechanism linking respiratory and cardiac fluctuations to BOLD fMRI is not yet known, but e.g. fluctuations in arterial CO_2 due to breath and pulse rate changes cause BOLD signal changes. Thus resting state fMRI analysis is complicated by unknown low-frequency noise sources, although at 1.5T physiologic noise is less pronounced compared to 3T scanners. Data-driven independent component analysis (ICA) can, in theory, separate spatiotemporally independent signal sources, like noise processes from neural processes, but capability has not been determined in the frame of RSNs, although at least task related independent components (IC) have been shown to be highly repeatable using odd and even timepoints of the original timeseries as input data (3). In this study, the relevance of the physiological noise correction for the ICA in detecting RSNs and especially DMN, is of interest.

Methods:

Subjects and imaging: Twelve healthy adults were imaged on GE 1.5T HDX scanner equipped with an 8-channel head coil. Volunteers were instructed to rest their eyes closed for the 7 min 24 s long BOLD fMRI scanning (GR-EPI, TR 1764 ms, TE 40 ms, flip angle 90, 4x4x4 mm voxel). Heart beats were recorded using photoplethysmograph and respiration data was measured using respiratory belt, both equipment provided by the scanner manufacturer.

Pre-processing: AFNI was used for motion correction and physiologic noise correction of the data. Dataset that is only motion corrected will be referred as *noCorr* and dataset that is also corrected for physiologic noise as *physCorr*. Physiologic noise correction constitutes of three different methods: 1) RETROICOR (4); slightly modified version of RETROICOR implemented in AFNI 3dretroicor function was performed. 2) Respiration volume per time (RVT) (1) using eight lagged regressors (from -6 TR (-10,5 s) to +15 TR (+26,5 s)) in deconvolution. 3) Correction for cardiac rate low-frequency fluctuation (2) using five lagged regressors (from 0 TR to + 15 TR (26.5 s)) in deconvolution. Three subjects had to be excluded from analysis due to too many spurious pulses (> 5%) (2). Altogether eight respiratory and five cardiac estimates were then regressed out from the BOLD timeseries and remaining residual constituted the *physCorr* data.

Analysis: Spatial ICA (FSL MELODIC) was performed for both *noCorr* data and *physCorr* data. Estimation of the number of components was performed for *noCorr* data. This estimate was used also for the *physCorr* data, since dimensionality estimation for *physCorr* data can result in several times more ICs to be calculated compared to *noCorr*. This is due to the regression analysis in the prior preprocessing that removes variance from the data. However, from the ICA viewpoint it seems to break the spatiotemporal integrity of the independent components. DMN ICs were visually identified from the *noCorr* ICA results and for every subject the best matching DMN pair from the *physCorr* ICA results was selected with the help of spatial cross-correlation. Additionally ICA was performed for the data that was obtained as a fit for physiological regressors to see what was regressed out. After spatial smoothing and normalization in FSL, unthresholded z-score DMN maps were fed into Wilcoxon signed-rank test to perform non-parametric paired comparison on group-level between the *noCorr* and *physCorr* DMNs.

Results and discussion:

DMN IC maps did not change significantly after physiological correction as illustrated by DMNs of the four representative subjects in Fig 1. On the other hand, performing ICA for the physiological regressors' regression fit (ICA on fMRI data *noCorr* minus *physCorr*) revealed IC maps with similar DMN characteristics (Fig. 1, bottom row) but weighted on the lower frequency than *noCorr* or *physCorr* DMN. Thus, regressing out lagged low-frequency respiratory and cardiac estimates, removes especially the low-frequency contribution of the respiratory and cardiac related noise sources from the DMN leaving spatial appearance quite similar. Difference between *noCorr* and *physCorr* DMN was found to be not statistically significant. In Fig 2, is shown the most significant difference (peak value t = 2.66) where *physCorr* DMN was greater than *noCorr*.

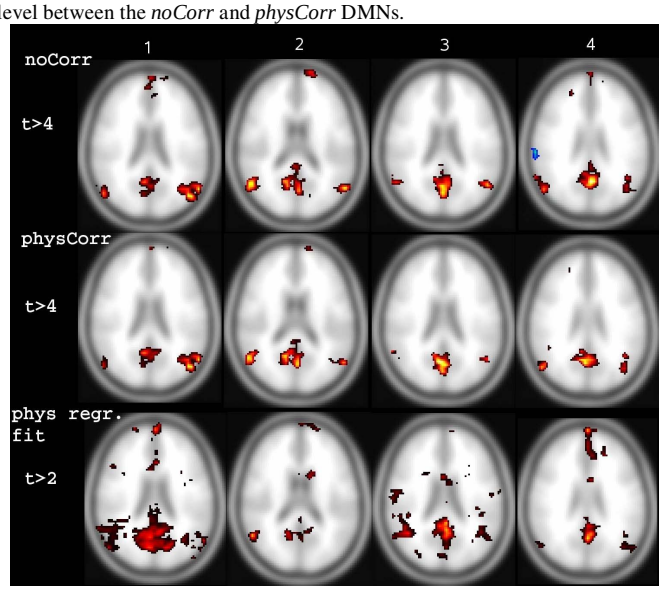

Figure 1. Default mode ICs of representative subjects.
Top: *noCorr* - normally pre-processed data (t>4).
Middle: *physCorr* - physiologically corrected data (t>4).
Bottom: ICA on physiological regressors' fit (fMRI data *noCorr* minus *physCorr),* lower threshold for illustration purposes (t>2), only positive side of the DMN-like IC is shown.

Conclusion:

Necessity of the physiological noise correction in fMRI analysis depends on the study focus; in spatial analysis ICA performance does not significantly benefit of physiological noise correction at 1.5T. If a study concerns the time or frequency domain of the RSNs, physiological correction would be benefitial.

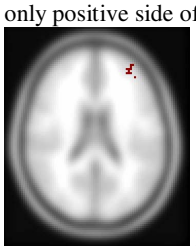

Figure 2. Group-level paired group comparison (N=9) of *noCorr* and *physCorr* DMNs. Threshold is uncorrected $p<0.01$ to illustrate the most meaningful difference.

References:

[1] Birn RM, Diamond JB, Smith MA, Bandettini PA. Separating respiratory-variation-related fluctuations from neuronal-activity-related fluctuations in fMRI. Neuroimage. 2006 Jul 15;31(4):1536-48.

[2] Shmueli K, van Gelderen P, de Zwart JA, Horovitz SG, Fukunaga M, Jansma JM, Duyn JH. Low-frequency fluctuations in the cardiac rate as a source of variance in the resting-state fMRI BOLD signal. Neuroimage. 2007 Nov 1;38(2):306-20.

[3] McKeown MJ, Makeig S, Brown GG, Jung TP, Kindermann SS, Bell AJ, Sejnowski TJ. Analysis of fMRI data by blind separation into independent spatial components. Hum Brain Mapp. 1998;6(3):160-88.

[4] Glover GH, Li TQ, Ress D. Image-based method for retrospective correction of physiological motion effects in fMRI: RETROICOR. Magn Reson Med 2000; 44:162-167.