A Bootstrap Method For Removing Aliased Cardiac and Respiratory Effects in Volumetric Resting State Connectivity Data

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Introduction:

Low frequency BOLD fluctuations (LFBF) are correlated between brain regions with a high degree of functional connectivity(1-3). In order to maintain a high degree of specificity in correlation between functional regions, it is necessary to remove the effect of cardiac and respiratory-related fluctuations(2). In rapidly sampled acquisitions (TR<400ms) this is accomplished through bandpass filtering(4). When volumetric data are acquired, the sampling rate necessarily drops below the rate at which cardiac and respiratory fluctuations are directly sampled and they will be aliased into the acquired data(5, 6). These aliased effects can punch through the 0.01-0.1Hz bandpass filter that is typically applied to LFBF data and dramatically reduce the specificity of the connectivity measurement(2). Recently, retrospective methods have been introduced to correct for these aliased effects using parallel, direct-sampled measures of cardiac and respiratory rates(7, 8). It is not always possible, however, for researchers to obtain this parallel information. In this study, we demonstrate that cardiac and respiratory rate effects exist in cortical tissue in undersampled acquisitions and propose a novel bootstrapping technique to correct for the effects retrospectively.

Methods:

It has been shown that large vessels in the brain are strongly coupled to cardiac and respiratory fluctuations(2, 4). Our hypothesis is that the signals from these large vessels can be used *in lieu* of a direct-sampled cardiac/respiratory signal as an estimator of the aliased effects.

The following data were acquired on 3 subjects using a Siemens 3T Trio MRI scanner with a birdcage RF coil.

Data Acquisition: :

Scan 1: 120 axial 3D MPRAGE images were acquired with TE/TR/flip=12ms/35ms/30^o , matrix=256x128, 256mm x 256mm FOV.

Scan 2: 256 volumes of 31-4mm thick axial slices were acquired using a prospective motion-controlled, gradient recalled echo, echoplanar acquisition with TE/TR/flip=29ms/2000ms/90^o , matrix=64x64, 256mm x 256mm FOV, receive bandwidth=125KHz. In parallel, pulse and respiratory information were acquired using the optical pulse plethysmograph and respiratory bellows provided with the scanner that are normally used for gating. The subject was instructed to remain at rest with their eyes closed.

Scan 3: same as Scan 2 except 160 volumes while executing a bimanual finger opposition task as a 32seconds rest/32 seconds tapping block-style paradigm.

Data Analysis: The data analysis for the resting state data proceeded in two stages, physiologic noise removal and correlation analysis.

Physiologic noise removal: Pulse and respiratory data were used to remove aliased fluctuations from Scan 2 using RETROICOR(7). We refer to this as the *pristine correction*. The pixel-by-pixel amplitudes of the correction waveform were recorded during the procedure. The middle cerebral arteries were identified from Scan 1 and an ROI was placed in the corresponding location in Scan 2. The averaged timeseries from this ROI was extracted and used as an estimator of the aliased physiologic effects. RETROICOR was performed again on Scan 2 using this estimator as the input correction waveform. We refer to this as the *estimated correction*.

Correlation Analysis: Both the pristine corrected dataset and the estimated corrected dataset were subjected to the same analysis. All data were first spatially filtered with a 2-dimensional Hamming filter(9). Scan 3 was analyzed for significant activation in the motor cortex. A least-squares fit of the reference function to the timeseries at each voxel is performed and a Student's t map is produced. A seed ROI is placed in the left hemisphere primary sensorimotor region for all subjects, as determined from significantly activated voxels from Scan 3. All timeseries from Scan 2 were bandpass filtered in the temporal frequency domain ([0.01,0.10Hz]). The timeseries from this region in both corrected datasets from Scan 2 were used as a reference function and the cross correlation to all voxels was calculated.

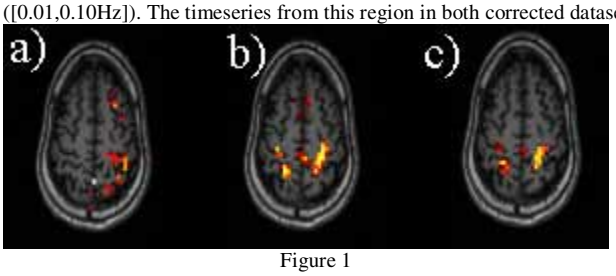

Figure 1

Results and Discussion

Figure 1a shows the pixels with the highest coupling to the cardiac rate in a slice containing primary SMC, as determined by RETROICOR. The fact that voxels in the left-hemisphere primary sensorimotor region (indicated with red arrow in Fig 1a) have high power is of concern. Without removing the cardiac-related fluctuations, the other regions with high coupling can have high correlation to our reference region, even after band-pass filtering. Figure 1b shows the pixels with highest correlation in LFBF to the seed region in left hemisphere in the dataset with the pristine correction applied. The observed correlation pattern outlining bilateral primary sensorimotor regions as well as the supplementary motor regions is a typical result and has been widely reported(1-3). Figure 1c shows pixels with hghest correlation to the same region using the estimated correction. The resulting connectivity map outlines the same homologous right hemisphere and medial motor regions as Fig 1b.

Conclusion

This study demonstrates that there are regions in cortical tissue that exhibit a strong coupling to aliased cardiac fluctuations. In addition, we have shown that the timeseries MRI signal from voxels with large vessels can be used to estimate and retrospectively remove the contribution of aliased physiologic noise in data that have undersampled these effects. This methodology offers a simple alternative for retrospective correction of aliased physiologic effects.

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