Reliability of the resting state fluctuation amplitude as a hemodynamic scaling parameter

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Introduction: BOLD fMRI responses to a neural task can vary across brain regions, sessions and subjects depending on the underlying cerebro-vasculature and basal conditions [1,2,3]. Though hypercapnia, induced through breath holding and CO_2 inhalation, has been used for vascular reactivity studies [4,5], it is disadvantaged by various concerns such as patient compliance, evoked neural activity and requirement of additional equipment for hemodynamic scaling [6]. Recently, we have observed high correlation between the resting state fluctuation amplitude (RSFA), breath hold response amplitude and CO_2 response amplitude and demonstrated the use of RSFA for hemodynamic scaling [7]. In this study, we have used the bootstrap resampling method to validate the use of RSFA as an alternative to hypercapnia-based scaling. Reliability of the correlation between RSFA, breath hold response amplitude and CO_2 response amplitude was evaluated by bootstrapping the BOLD-fMRI time series. Stability of the correlation between RSFA, breath hold response amplitude and CO_2 response amplitude was evaluated by bootstrapping varying lengths of the BOLD-fMRI time series.

Methods:Experiment: Eight healthy subjects (5 males) were scanned on a 3T Siemens Allegra (Siemens, Ehrlagen, Germany) imaging system. All subjects performed bilateral finger tapping and breath hold (end-inspirational breath-hold of 25 seconds) paradigms. Four subjects also performed the CO_2 inhalation (5% CO_2) paradigm. The finger tapping, breath hold and CO_2 breathing paradigms consisted of alternating periods of 25 seconds of respective task and 50 seconds of rest. Rest scans were obtained for all the subjects. Single shot gradient recalled echo – EPI images (TR/TE = 1000/30 msec, FOV=22cm, 64x64x6 matrix, slice thickness= 7mm, FA=80^o, 250 time-points) were obtained during each task.

Analysis: The EPI images were corrected for motion and quadratic trends were removed. Standard deviation (SD) of the voxel time course was used as a measure of signal variability. The SD during the resting condition determined RSFA while the SD during breath hold and CO_2 determined the extent of BOLD signal change due to the hypercapnia tasks. Maps of the SD were obtained for rest, breath hold and CO_2 breathing paradigms and were subsequently correlated with one another on a voxel by voxel basis. To evaluate reliability of the correlation of RSFA and hypercapnic (breath hold or breathing CO_2) response amplitude the bootstrap resampling method was used. The time series in each voxel over all experimental conditions were resampled once resulting in a new 'pseudo' time series containing 210 points and the same distribution as that of the original time series. The SD was estimated from the 'pseudo' time series for each experimental condition. The resulting SD estimate was cross-correlated with the corresponding voxel SD of another condition (i.e. rest v/s breath hold, rest v/s CO_2, and CO_2 v/s breath hold) yielding one correlation coefficient value for each comparison. This procedure was repeated 5000 times for all experimental conditions resulting in a distribution of 5000 correlation coefficient values for each comparison between experimental conditions. The mean and SD of the resulting distributions were calculated. To evaluate the stability of the correlation between RSFA, breath hold response amplitude and CO_2 response amplitude, the bootstrapping procedure was applied for different lengths of the time series. The length of the time series was varied from 30 points to 250 points in steps of 30 i.e., 30, 60, 90, 120, 150, 180, 210, and 250. The distribution of the correlation between RSFA, breath hold response amplitude and CO_2 response amplitude for various time series lengths were obtained. The mean and SD of these distributions were calculated and plotted against the number of points in the time series.

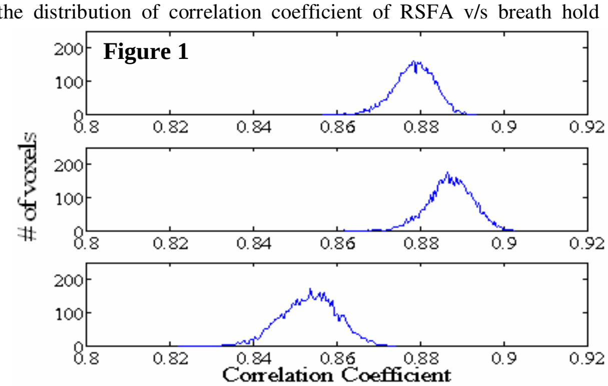
Results & Discussion:

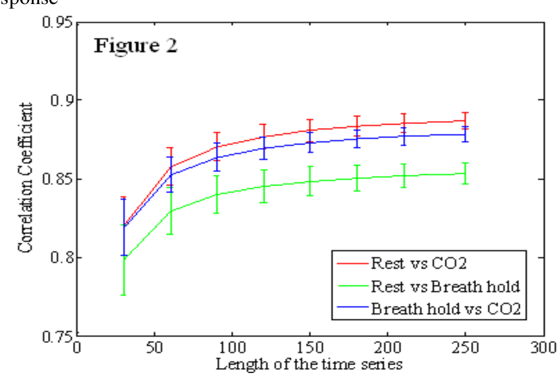
The correlation among RSFA, breath hold and CO_2 response amplitude was high ($R>0.8$) for all subjects. The correlation decreased after removal of outliers for all the three cases, however no significant change was observed for all subjects except two. We tested the reliability of the correlation using bootstrap resampling. As observed in Table 1, SD of the distribution of correlation coefficient obtained after bootstrap resampling was low for all subjects. Figure 1 A, B, and C shows the histogram of the correlation coefficient of breath hold response amplitude v/s CO_2 response amplitude, RSFA v/s breath hold response amplitude, and RSFA v/s CO_2 response amplitude, respectively, obtained after bootstrap resampling. The distributions after bootstrapping were very similar. This indicates that the high correlation between RSFA, breath hold response amplitude and CO_2 response amplitude was not affected by high amplitude in certain outlying voxels during the different experimental paradigms.

Table 1. Mean ± SD of the distribution of the correlation between RSFA, breathhold, and 5% CO_2 response after bootstrap resampling.

Subject	Breath hold vs 5% CO_2	RSFA vs Breath hold	RSFA vs 5% CO_2
1	0.876 ± 0.005	0.851 ± 0.008	0.885 ± 0.006
2	0.901 ± 0.025	0.870 ± 0.025	0.916 ± 0.007
3	0.875 ± 0.013	0.710 ± 0.015	0.662 ± 0.011
4	0.948 ± 0.003	0.871 ± 0.008	0.894 ± 0.007
5	----------	0.766 ± 0.016	----------
6	----------	0.750 ± 0.011	----------
7	----------	0.848 ± 0.011	----------
8	----------	0.860 ± 0.010	----------

We tested the stability of the correlation by varying the length of the time series. Figure 2 shows the plot of mean ± SD of the distribution of correlation coefficient of RSFA v/s breath hold response amplitude, RSFA v/s CO_2 response amplitude, and breath hold response amplitude v/s CO_2 response amplitude with various lengths of the time series in a typical subject. No significant change was observed in the mean and SD of the distribution of correlation coefficients when more than 60 time points were considered (figure 2). A similar trend was found for the remaining subjects. Thus reducing the length of the time series, or residual motion induced artifacts and slow signal drifts after correction does not seem to play a significant role in the observed high correlation between RSFA, breath hold response amplitude and CO_2 response amplitude.





Conclusion: We have shown that the observed high correlation of RSFA with the amplitude of breath hold or CO_2 response in healthy subjects is reliable and stable. The use of RSFA for hemodynamic scaling would not only avoid the shortcomings of the hypercapnia stimulus but also eliminate the need for several additional tasks in the MR-scanner. A reliable correlation between RSFA, breath hold response amplitude and CO_2 response amplitude during partial consideration of the time series, suggests that the resting state acquisition of just 60 time points prior to the onset of the task would be sufficient for hemodynamic scaling hence eliminating an additional resting state scan.

References:

1) Bandettini and Wong, NMR Biomed 10(4-5), 197-203,1997; 2) Cohen et al., JCBF 22 (9), 1042-53, 2002; 3) Handwerker et al., Neuroimage 21 (4), 1639-51, 2004; 4) Kastrup et al., MRM 42 (3), 608-11, 1999; 5) Brown et al., JCBF 23 (7), 829-37, 2003 6) Corfield et al., J Physiol 488 (Pt 1), 77-84,1995 7) Kannurpatti and Biswal, Neuroimage [Epub ahead of print], 2007.