Hypercapnic scaling of task induced fMRI BOLD signals and its dependence on task design

S. S. Kannurpatti[1], M. Motes[2], B. Rypma[2], and B. B. Biswal[1]

[1]Radiology, UMDNJ-New Jersey Medical School, Newark, New Jersey, United States, [2]Behavioral and Brain Sciences, University of Texas at Dallas, Dallas, Texas, United States

Introduction: Blocked and event related stimulus designs are typically used in fMRI studies depending on the importance of detection power or estimation efficiency. The extent of vascular contribution to variability in blocked and event related fMRI-BOLD response is not known. Using hypercapnic scaling, the extent of vascular weighting in the fMRI-BOLD response during blocked and event related design paradigm was investigated. BOLD data from healthy volunteers performing a blocked design motor paradigm and an event related memory paradigm that needed the performance of a motor task were analyzed from the region of interest (ROI) surrounding the primary and supplementary motor cortices.

Methods: 24 healthy human subjects (11M and 13F; mean age: 41 years; range: 19-71 years) with no history of head trauma and neurological disease were scanned in a 3T Philips MR-scanner. The Institutional Review Board of the University of Texas at Dallas approved all experimental procedures. Each subject performed a breath hold (BH), bilateral fingertapping (FTAP) or Digit-Symbol Substitution task (DSST) paradigm. The MR scanner was equipped with a fixed asymmetric head gradient coil and a quadrature transmit/receive birdcage radio-frequency coil. Foam padding and a pillow were used to minimize subject head motion. High-resolution T1 weighted anatomical images were obtained from all subjects using an MPRAGE sequence. Gradient echo-EPI images were subsequently obtained during rest, BH, FTAP and the DSST task. 32 slices were obtained in the axial plane covering the entire brain. Imaging parameters were: FOV of 22 cm, matrix size of 64x64, TR/TE = 2000/30 msec and slice thickness of 4mm. To determine activated areas during each task, a gamma-variate function was convolved with the task reference function and cross correlated with the BOLD signal on a voxel-wise basis. Group activation maps were determined by converting each subject's functional map to standard stereotaxic space based on the Talariach and Tournoux atlas using a linear transformation. The correlation coefficients 'r' from each individual subject's functional maps were z-transformed by considering the arctanh of 'r' on a voxel-wise basis. The z-transformed map from each subject was averaged and transformed by considering the tanh of the z-values to obtain the average correlation coefficient map for each group. Three regions of interest (ROIs) were defined covering the left and right primary motor cortices and the supplementary motor area using significantly active voxels ($P<0.01$) from the group map in response to the blocked design motor task. All further analysis was carried out within this defined ROI. Hemodynamic amplitude scaling was accomplished by dividing the BOLD signal response amplitude during the task (FTAP or DSST) with the BH-induced BOLD response amplitude or the Resting State BOLD Fluctuation Amplitude (RSFA) in the corresponding voxels.

Results and Discussion: To define the ROIs, a logical union map of the active voxels from all subjects performing the blocked design motor task was obtained using a threshold of $P<0.01$. ROIs were drawn enclosing all active voxels in the logical union map (Fig 1A). These ROIs included the primary and supplementary motor cortices and parietal areas of the brain. There was variation in the spatial extent of activation during the blocked design motor task with certain older subjects indicating activity in the parietal areas during the performance of the blocked design motor task. Thus the ROIs maximized the inclusion of active voxels during the blocked design task from all subjects by including some of the parietal areas. Further analysis of the BOLD data from subjects performing a blocked and event related tasks were done from the same ROIs. As observed from the group activation maps, the spatial extent of activation in the primary motor cortex was substantially higher during the blocked design paradigm compared to the event related. The supplementary motor cortex was however activated more during the event related task (Fig 1B,C).

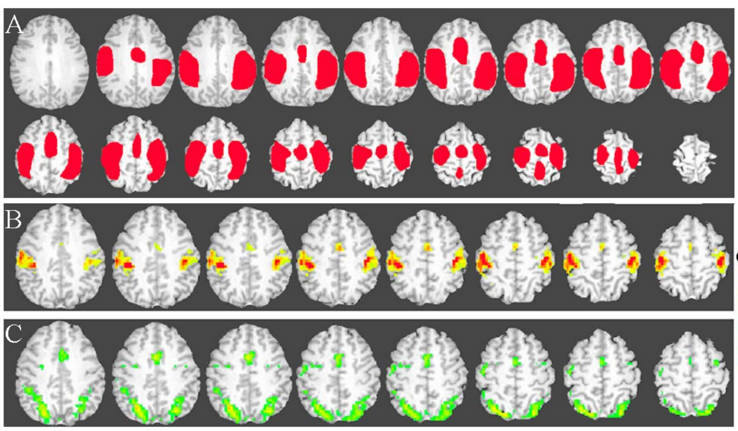

Fig 1

As shown in fig 2A, the mean BOLD signal change estimated from all active voxels in the ROIs over all subjects was 1.85±0.42% during the blocked design task and significantly larger than 0.97±0.20% observed during the event related task (Student's t-test; $P<9\times10^{-12}$). Scaled fMRI responses were obtained by dividing the task-induced response in each voxel by the corresponding BH response and RSFA estimates. Hypercapnic scaling of the blocked design response using RSFA significantly reduced the average BOLD signal change to 1.46±0.28% (compared to the unscaled response; Student's t-test; $P<3\times10^{-4}$) while the event related response scaled with RSFA significantly reduced to 0.85±0.18% (compared to the unscaled response; Student's t-test; $P<0.02$) (Fig 2B). Hypercapnic scaling of the blocked design response using BH significantly reduced the average BOLD signal change to 1.03±0.19% (compared to the unscaled response; Student's t-test; $P<5\times10^{-10}$), while the event related response scaled with BH reduced to 0.75±0.18% (compared to the unscaled response; Student's t-test; $P<2\times10^{-4}$) (Fig 2C).

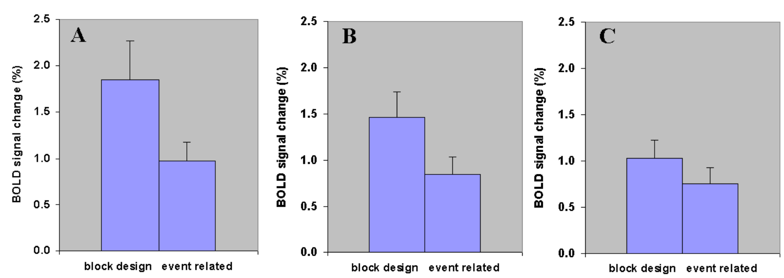

Fig 2

The BOLD signal variability within each subject was calculated as the ratio of the SD and mean BOLD signal change within the ROI defined as the spatial coefficient of variation (CV_s). During the block design task, the CV_s prior to scaling was 1.23, which reduced to 1.14 and 0.39 after hemodynamic scaling with RSFA and BH respectively (Fig 3A). During the event related task, CV_s prior to scaling was 0.39, which showed no significant change after scaling with RSFA and decreased slightly after scaling with BH (Fig 3B). These results indicate that in every subject, BOLD signal change within the same cortical system can vary considerably more during a blocked design task compared to event related. Further, hemodynamic scaling with RSFA and BH significantly decreased the spatial variability in the BOLD signal only during the blocked design task. This indicates a strong vascular weighting in the BOLD signal variability within the motor cortex during the blocked design task.

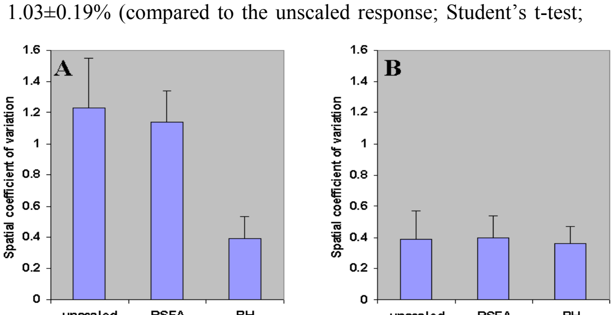

Fig 3

Conclusion: Sparse vascular variability during the event related task compared to the blocked design indicates that BOLD variability is dependent on the type of task design. In fMRI studies investigating neural function in normal aging and diseases where vascular properties can alter, the event related design would be the most suitable as there would be lesser BOLD variability from vascular sources.