Performance of capnia-derived regressors for ASL measurement of cerebral vasoreactivity to circulating gases

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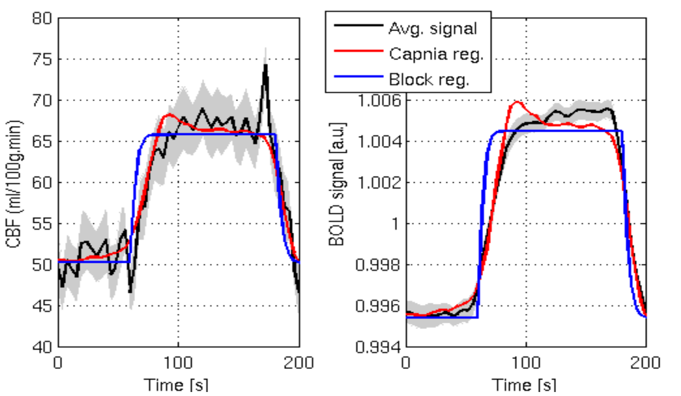
Introduction

Robustly measuring cerebral vasoreactivity to circulating gases in patients may provide valuable diagnostic information or insight into pathophysiological processes in a variety of diseases [1]. MRI methods are increasingly used, combining modulation of capnia with dynamic imaging of perfusion either via ASL [2] or indirectly via the BOLD signal. The correlation of the observed fMRI signal with a regressor modeling the response to changes in capnia is then used as a local measure of cerebral vasoreactivity. A challenge in such studies is to correctly model the signal modulation occurring during the task, which may depend on subject compliance and individual variability in the response to the capnic challenge. This is especially critical in ASL with its limited SNR, as any mismatch will further decrease sensitivity. This has been addressed either via the use of open- or closed-loop systems aiming to generate vasoactive stimuli closely following a block paradigm [3], via exclusion of data obtained during the transition periods between capnia states, or via the use of empirical population-average regressors [1]. Here we assess the performance of regressors derived from hypercapnia data collected during each scanning session for the analysis of ASL data. The method has been applied to BOLD data previously [4], but its performance has not been compared to other regressors to our knowledge. This approach potentially circumvents the need for cumbersome gas administration equipment or high patient cooperation during a breath-hold task, while providing robustness to experimental variability.

Materials and Methods

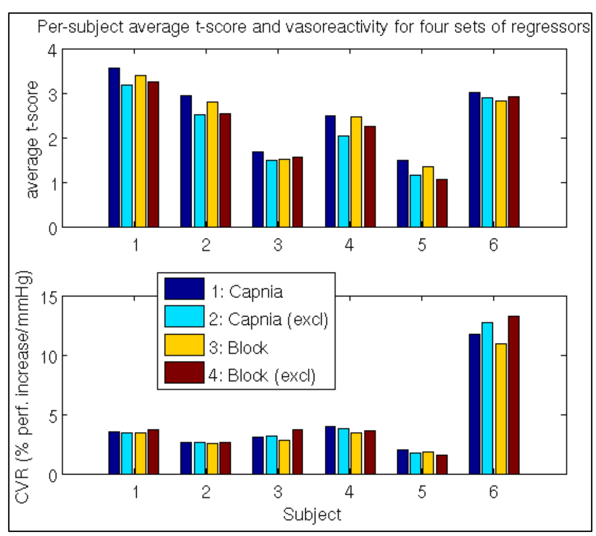
Four healthy volunteers (23±2 years) and two patients (arterio-venous malfunction and a stroke patient, day 15) were examined in a Philips Achieva 3T Tx system using protocols approved by the local ethics committee. Acquisitions, performed with a 32-channel head-only receive array, included a T_1-weighted structural image, an ASL reference scan and one series of pseudo-continuous ASL data [5] (WET pre-saturation, 1650 ms label, 1525 ms post-label delay) using a multi-slice single-shot EPI readout (3x3x6 mm^3, 20 slices, TE 12 ms, sense 2.5) with a TR of 4 s for a duration of 12 min. Capnia was modulated in a 1/2/1 min paradigm (3 cycles) by alternating air and an air/CO_2 mixture (7% CO_2, 21% 0_2, balance N_2) administered at 12 l/min via a high-concentration face mask. End-tidal CO_2 was measured via nasal cannula using an MR-compatible capnometer, and recorded together with scanner triggers for synchronization. Data were analyzed using Matlab, the SPM software and custom routines. Images were realigned after removing any systematic bias in realignment parameters between tag and control images. Frames exhibiting strong motion were marked for exclusion from the subsequent analysis. Structural images were segmented and all images were normalized to the MNI template. Functional data were smoothed in 3D using an 8-mm Gaussian kernel. ASL signal amplitude was scaled to express the difference between control and tag images in units of ml/100g.min.



Outliers in hypercapnia data were discarded and data were interpolated to the pCASL volume acquisition times, taking lag due to dead space in the sample line into account. The average of capnia values below the median value was considered 'baseline'. Baseline perfusion was modeled with a 'constant' regressor alternating between 0.5 and -0.5 for control and tag images respectively throughout the scan. Four different sets of regressors for hypercapnia-related perfusion and BOLD signal changes were constructed : One proportional to the baseline-corrected capnia data ('Capnia') (ctl/tag modulated for perfusion, unmodulated for BOLD), one in a standard block design ('Block'). All regressors were convolved with an HRF exhibiting no undershoot (FWHM = 10 s). Two additional analyses were performed, excluding for both regressors data acquired within 32 s after each change in capnia state. For each scan, an ROI was defined including all voxels with a gray-matter fraction of at least 70% in which significant baseline perfusion was detected for all four sets of regressors ($p<0.05$ FWE). ROI-average t-score and response amplitudes were computed for each model and all subjects. Fig. 1 shows average demodulated unfiltered ASL and BOLD signals as well as the average of the regressors used.

Results

All regressors adequately modeled the data in this limited dataset, with only minute differences. The capnia regressor produced on average 5% higher t-scores than the block regressor, a small difference with respect to the variability of t-scores within the ROI but highly significant ($p<0.001$) for all subjects but one, given the large number of voxels sampled. Excluding frames during the transition periods reduced the t-score by 12% for the capnia regressors and by 5% for the block regressors. The reduction in t-score expected from the loss in degrees of freedom alone is 14%, indicating that signal during the transition periods was well modeled by the capnia regressor. Ignoring transition periods did not affect the response amplitude for the capnia regressors but increased the measured response by 8% for the block regressors. CVR values measured were in normal range for the healthy subjects. The unusually large CVR calculated for the stroke patient stems from low observed $etCO_2$ values. The resulting capnia regressors still modeled the response well and provided useful relative CVR maps, albeit with an overall scaling.



Discussion & Conclusion

In the present study, regressors derived from individually collected capnia data consistently outperformed block-design regressors, even though the gain in significance was small compared to regional or subject variability. The temporal signal, including transitions between baseline and hypercapnia, was better modeled than by the block regressor, more than compensating any variability inherent in the capnia measurement. It is expected that capnia-derived regressors are more forgiving to experimental variability such as timing of the manually switched valves or patient respiratory response to hypercapnia than traditional block designs, and thus to be useful to further increase robustness of ASL vasoreactivity measurements in the clinic.

References [1] Jiang et.al. NIMG **52**:538,2010; [2] Nöth et.al. JMRI **24**:1229,2006; [3] Slessarev et.al. JPhysiol **581**:1207,2007; [4] Yezuvath et.al. NMRBiomed **22**:779,2009; [5] Dai et.al. MRM **60**:1488,2008