Performance of capnia-derived regressors and physiological noise correction for ASL measurement of cerebral vasoreactivity to circulating gases

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Target audience: Neuroradiologists, Methodologists

PURPOSE

Robustly measuring vascular function in patients is of major interest as it may provide valuable diagnostic information or insight into pathophysiological processes in a variety of diseases. One way to assess vascular function is to measure cerebral vasoreactivity (CVR) via the dynamic observation of cerebral blood flow using ASL during experimental modulation of perfusion using hypercapnia [1]. Our aim is to compare the performance of a variety of data analysis methods in order to maximize the robustness of ASL CVR mapping in the context of clinical exams and basic and clinical research. Here, we analyzed ASL signal in a simple general linear model (GLM, [2]) where the model weight of a regressor predicting the response to changes in capnia is used as a local measure of cerebral vasoreactivity. The response model can be either a standard block paradigm based on the CO_2 administration periods or based on the capnic response measured via physiological monitoring of the subject during the exam [3]. We also analyzed the effect of excluding data obtained during the transition periods between capnia levels, and of regressors modeling physiological noise [4].

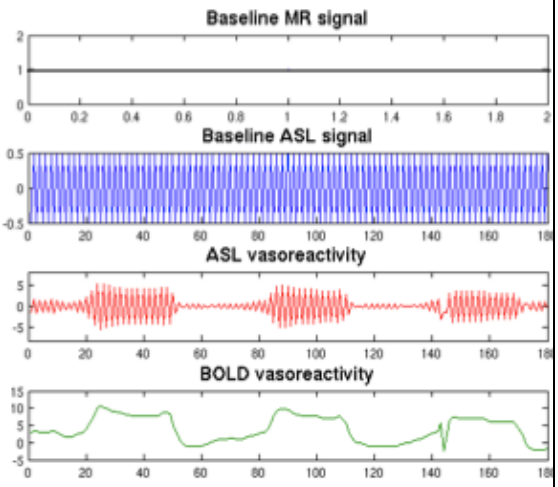

Figure 1: Exemple of regressors based on capnia

METHODS ASL vasoreactivity data from 39 patients and healthy volunteers (27 males, 11 females) were analyzed (66 sessions in total): 7 stroke patients followed at different timepoints (22 sessions), 13 severe stenosis patients (13 sessions), 19 healthy subjects (31 sessions). Data were acquired on a 3T Philips Achieva TX scanner using 8 or 32-channel receive arrays: T_1-weighted structural scan; one series of pseudo-continuous ASL data [5] (1650 ms label, 1525 ms post-label delay, multi-slice single-shot EPI readout, 3x3x6 mm^3 voxels, 20 slices, TR/TE 4000/12 ms, sense 2.5, total acquisition time 12 min); ASL reference scan; rapid T_1 map for CBF quantification. Capnia was modulated in a 1/2/1 min paradigm (3 cycles) by alternating administration of medical air and an air/CO2 mixture (7% CO_2, 21% O_2, balance N_2) at 12 l/min via a high-concentration face mask. End-tidal CO_2 ($EtCO_2$) and respiration were monitored via nasal cannula (Maglife, Schiller Medical). Cardiac signals were monitored using a pulse oximeter. Scanner TTL pulses were recorded to synchronize the physiological data to the ASL images. 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. Individual frames exhibiting strong motion were excluded from the analysis. Structural images were segmented and all images were normalized to the MNI template. Two types of vasoreactivity regressors were built for the general linear model (GLM) analyses: a block regressor based on CO_2 administration periods scaled to the capnia increase ("block") and a regressor proportional to the baseline-corrected $etCO_2$ data ("phys") (ctl/tag modulated for perfusion, unmodulated for BOLD). The full set of "phys" regressors is shown in Fig. 1. Six analyses were performed on each of the two regressors (12 analyses in total): 1) Capnia or block regressor only, 2) Exclusion of the data acquired within 32 s after each change in capnia state ("excl"), 3 to 6) Modeling of cardiac noise using retroicor [4] with regressors of cardiac ("card") or respiratory ("resp") phase at base and 1st harmonic frequencies for both ctl and tag images, or ctl/tag separately ("card/resp_split"). For each session, response amplitudes and t-scores were averaged over all voxels within healthy gray matter (GM fraction > 90%) with significant baseline perfusion in all analyses ($p<0.05$ FDR).

RESULTS Of the 66 sessions, 10 were excluded (problems during physiological data recording, subject movements), leaving 56 sessions for the analysis. CBF values are significantly different if data during transition periods is excluded from the analysis (Fig. 2). The mean CVR value in healthy gray matter is always greater using the physiological regressor (Fig. 2). The mean CBF T scores are always higher using physiological regressor compared to the block. Cardiac and respiratory noise correction improves the significance of CBF but has no impact on the significance of CVR (Fig.3). Exclusion of the transition periods decreases the significance of both CBF and CVR measurements (Fig. 3).

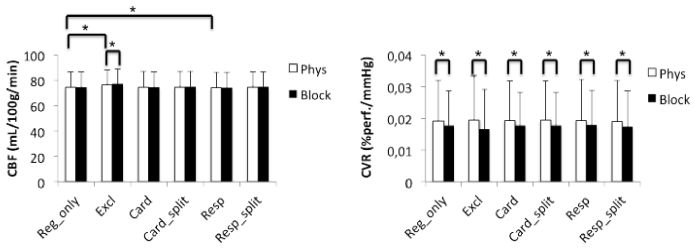

Figure 2: Mean CBF (ml/100g/min) and CVR (% perf. increase/mmHg) in 56 sessions for the six different analysis methods.

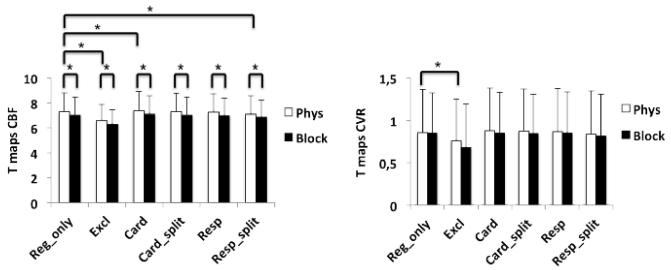

Figure 3: Mean T-scores for CBF and CVR measurements in 56 sessions for the six different analysis methods.

DISCUSSION & CONCLUSION Regressors derived from individually collected capnia data consistently provide higher SNR than block-design regressors in CBF measurements. 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 (data not shown). 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] Nöth, U., et al., 2006. J Magn Reson Imaging 24, 1229–1235. [2] Mumford, J.A., et al., 2006. 33, 103–114. [3] Yezhuvath, U.S., et al., 2009. NMR Biomed 22, 779–786. [4] Restom, K., et al., 2006. Neuroimage 31, 1104–1115.