Mapping of Hypercapnia Induced Cerebrovascular Reactivity using BOLD MRI

F.H.R. van der Zande, P.A.M. Hofman, H.G.J. Boere and W.H. Backes
University Hospital Maastricht, Dept. of Radiology, Maastricht, The Netherlands

Abstract
In 13 healthy volunteers, BOLD MRI scans, acquired during a hypercapnic stimulus without specific breathing instructions, showed a high percentage signal change in grey matter with a strong linear correlation to CO_2. Symmetrical images of low standard deviation, covering the entire grey matter, indicate the feasibility to detect exhausted cerebrovascular autoregulation.

Introduction
Reduced cerebral perfusion pressure has long been suspected as a risk factor for ischemic stroke [1,2]. This is reflected by reduced cerebrovascular reactivity (CVR) and increased oxygen consumption rate, known as "misery perfusion" [3]. Measurement of cerebral flow parameters alone is not sufficient to assess cerebral hemodynamic status. A vasodilative stimulus needs to be applied to test for remaining autoregulatory vasodilation. Doppler ultrasound provides data with poor spatial resolution; only blood flow velocity in the middle cerebral artery is measured. PET, Xenon-CT and SPECT are less widely available and also have major drawbacks. Only a few authors report the use of fMRI methods to investigate CVR [4,5]. We used a BOLD fMRI technique to assess the cerebrovascular reserve capacity during a rapidly alternating hypercapnic challenge.

Methods
Thirteen healthy volunteers were scanned for 12 minutes while inhaling alternating gas mixtures: high CO_2 mixture (7% CO_2 + 93% O_2) alternating with pure O_2 every 2 minutes. The transition speed between high CO_2 mixture and pure O_2 was increased by using a special breathing device which forces rebreathing during the high CO_2 state [5]. No specific breathing instructions regarding ventilation rate or volume were given. The functional scans were performed on a 1.5 Tesla MR scanner (Philips Intera), using a 3D T2* BOLD sequence with parameters: TR 26.1ms, TE 7.9ms, flip angle 9°, matrix 64x64, 30 contiguous slices and voxel size 3.5x3.5x3.5 mm^3. In 6 subjects additional 3D T1-FFE dynamic scans were made during an identical CO_2 paradigm. Dynamic T1 parameters: TR 13.4ms, TE 5.9ms, flip angle 35°, matrix 128x128, 12 contiguous slices positioned above the ventricles with 3.5x3.5x3.5 mm^3 voxel size. This sequence is sensitive to inflow of unsaturated blood due to its short TR. High resolution T1-FFE anatomical images were acquired for co-registration. End tidal pCO_2 ($p_{ET}CO_2$) was recorded continuously during MRI acquisition. The SPM software package was used to segment grey matter. Data were post-processed using linear modeling with the $p_{ET}CO_2$ as an explanatory variable. Statistical analysis was carried out using FMRIB-FSL [6].

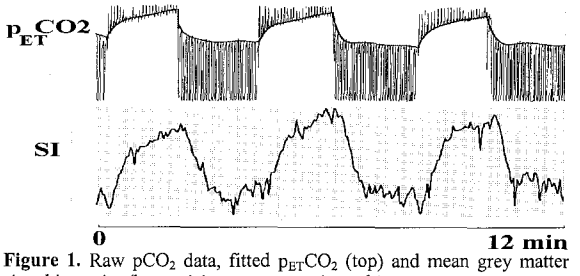

Figure 1. Raw pCO_2 data, fitted $p_{ET}CO_2$ (top) and mean grey matter signal intensity (bottom) in a representative subject.

Results
All subjects (7 female, mean age 29 y., range 20-47 y.) tolerated the experiment with minimal discomfort, the only complaint being an increased breathing resistance during the high CO_2 state. All experiments produced usefull data. Typical $p_{ET}CO_2$ values ranged from 35 to 55 mmHg with mean high and low CO_2 state values of 52 and 38 mmHg respectively. The $p_{ET}CO_2$ curves had a comparable shape in all subjects (Fig. 1). For each subject, the signal intensity curves were time-shifted (stepsize 3s) until a maximum coefficient of correlation with the corresponding $p_{ET}CO_2$ curve was found (mean r-value 0.91). The mean time shift to maximum correlation was found to be 12.7s (range 6-15s). A linear relationship was found between $p_{ET}CO_2$ and mean GM signal intensity with a slope of 0.8 ($p<0.001$) and no saturation effect (Fig. 2).

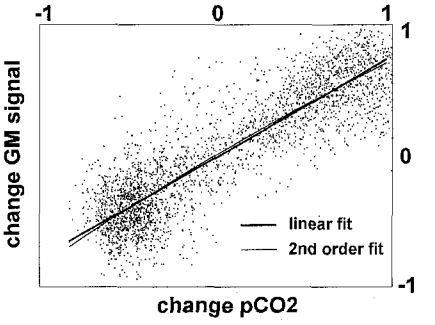

Figure 2. Curve fitting of group data shows a strong linear relationship between $p_{ET}CO_2$ and grey matter signal intensity.

The maps of mean percentage signal intensity and standard deviation show symmetrical images, as expected in healthy subjects (Fig. 3). The maximum change in GM signal intensity between the high and low CO_2 state is 9% with an average of 2.4%. Analysis of the dynamic T1 scans revealed a marked signal change (30-80%) in highly vascularized regions such as insula and cingulate (Fig. 3).

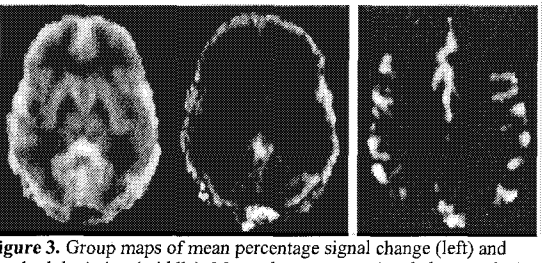

Figure 3. Group maps of mean percentage signal change (left) and standard deviation (middle). Mapped percentage signal change of T1 dynamic scan at a higher level in a representative volunteer (right).

Conclusions
Mapping of CVR using a hypercapnic stimulus is feasible without any specific breathing instructions, therefore, patients may tolerate the experiment well. A strong linear correlation between $p_{ET}CO_2$ and percentage signal change in grey matter was found for a wide range of CO_2 values. The mean time delay between hypercapnic stimulus and MR signal change is twice as long as in activation studies. Percentage signal change values are 2 to 8-fold higher than in activation studies. The symmetry and homogeneity in signal change of the entire grey matter and the low SD values indicate the feasibility to detect asymmetry in patients with unilateral exhausted cerebrovascular autoregulation. T1 dynamic scans confirmed the flow-mediated response to a hypercapnic stimulus.

References
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