Grey & White Matter Cerebrovascular Reactivity Response to Hypercapnia at 3 & 7T

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Introduction: Mild Hypercapnia induces vasodilation and increased cerebral blood flow (CBF), without changing oxygen metabolism[1]. Mapping cerebrovascular reactivity (CVR) to hypercapnia is important both clinically[2] and to improve understanding of the haemodynamic properties of the BOLD effect. This study compares measurements of CVR in grey matter (GM) at 3 and 7 T. A high precision system that controls expired end-tidal partial pressure of CO_2 and O_2 ($P_{ET}CO_2$ and $P_{ET}O_2$) independently was used to ensure CVR is assessed in response to CO_2 changes alone. Rapid monitoring of the $P_{ET}CO_2$ with this system allowed CVR maps to be produced based on *actual* hypercapnic level at each time point rather than *prescribed* level of hypercapnia.

Method: The study was performed on five healthy male subjects (aged 25±3 years). Hypercapnic challenges were achieved using a prospective, feed-forward, low gas flow system (RespirAct™, Thornhill Research Inc., Toronto, Can.), which allowed independent control of $P_{ET}CO_2$ and $P_{ET}O_2$ levels. Hypercapnic challenges were presented in the pseudo-randomised order. Three minutes of baseline $P_{ET}CO_2$ (40 mmHg) were followed by five cycles of a 2 minute CO_2 challenge (49, 43, 37, 40 and 46 mmHg $P_{ET}CO_2$) and 1 minute of baseline. $P_{ET}O_2$ was maintained at 100 mmHg throughout. Scanning was performed on a Philips Achieva 3.0T system, with a volume transmit and 8-ch SENSE receive coil, and a Philips Achieva 7.0T system, with volume transmit and 16-ch SENSE receive coil. Axial images were acquired using a double-echo EPI sequence (TE = 16/81 ms at 3T and TE = 20/57 ms at 7T), 192x192 mm FOV, 2x2x3mm^3 voxel with 9/10 slices (3T/7T), with no slice gap, in a TR of 1.5 s. Inversion-recovery EPI images with GM, white matter (WM) and CSF nulled in turn were acquired with the same geometry for tissue segmentation, and a high-resolution (0.8mm isotropic) T_2*-weighted image was acquired at 7T for vein segmentation. FSL (FMRIB, Oxford, UK) was used for realignment, brain extraction and GM segmentation. R_2* was calculated on a voxel-by-voxel basis, using a linear fit. Breath-by-breath $P_{ET}CO_2$ was linearly interpolated and manually shifted to align with a T_2* timecourse, averaged over all GM and WM voxels separately. This allowed the actual level of hypercapnia and the R_2* (averaged over all GM) to be compared on a point-by-point basis (rather than simply comparing the signal change to the prescribed level of hypercapnia). To increase SNR, CVR maps were generated by the weighted summation[3] of the normalized signals at each echo time on a voxel-by-voxel basis.

Results: The R_2* timecourses closely followed the $P_{ET}CO_2$ timecourse at both field strengths (fig.1). The $P_{ET}O_2$ levels were maintained within ±2 mmHg throughout the paradigm. Average GM R_2* reactivities agreed well between subjects (fig 2): 0.074±0.007 $s^{-1}mmHg^{-1}$ at 3T and 0.145±0.020 $s^{-1}mmHg^{-1}$ at 7T. R_2* reactivity is 2.0±0.4 times higher at 7T than at 3T. CVR maps show that significant reactivity is found in GM at both field strengths (fig. 3). The paradigm provided enough sensitivity to detect the average WM R_2* reactivity; 0.022±0.013 $s^{-1}mmHg^{-1}$ at 3T and 0.042± 0.015 $s^{-1}mmHg^{-1}$ at 7T.

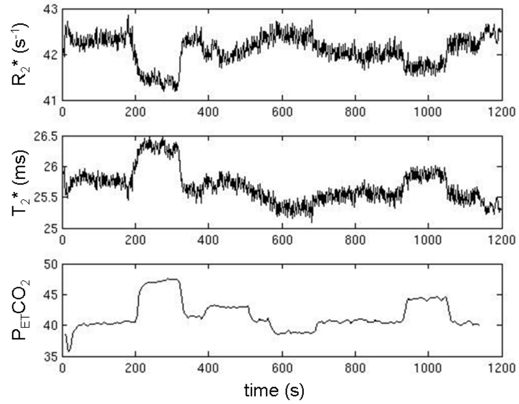

Figure 1: Tight correlation between grey matter timecourses and $P_{ET}CO_2$.

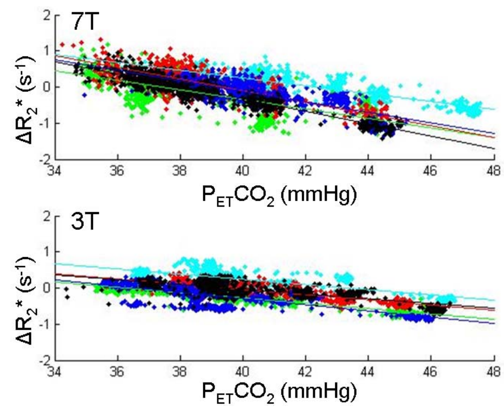

Figure 2: GM averaged R_2* reactivity at 3 and 7T.

Discussion: This study presents a cross-field comparison of the MR assessment of CVR in response to graded hypercapnia. A linear correlation was found between changes in GM R_2* and $P_{ET}CO_2$ over the range of $P_{ET}CO_2$ studied. The point-by-point temporal analysis improved sensitivity in CVR (by reducing errors due to the differences in the prescribed and actual levels of $P_{ET}CO_2$) to such an extent that WM reactivity was detected, this will allow the use of smaller steps in $P_{ET}CO_2$ which will be more acceptable to patients. Good control over blood oxygenation during hypercapnia gave confidence that reactivity was purely due to CO_2 changes and not O_2 changes. R_2* reactivity increased with field strength, which is consistent with previous cross-field studies[4]. The high resolution used in this study compared to previous studies[2,4] reduced physiological noise and partial volume effects. GM R_2* reactivity changes found in this study agree with the prediction of a 2.3-fold increase in ΔR_2* between 3 and 7T, for a simple physiological model[5]. Although better contrast was achieved at 7T, similar contrast-to-noise was observed at both field strengths in GM due to hardware limitations leading to use of non-optimal TE at 7T and increased physiological noise. Current work is investigating the use of RETROICOR on this data since physiological noise will be particularly high in this paradigm which involved the subject taking relative large regular breaths. Future work will use this paradigm in clinical studies of cerebrovasular disease[2] and will use the respiratory challenge to compare CBF and blood volume changes.

References: 1. Hoge, R. *et al.*, Magn. Res. Med. 42: 849 (1999) **2.** Van der Zaande, F. *et al.*, Neuroradiology 47:114 (2005) **3.** Posse, S. *et al.*, Magn. Res. Med. 42: 87 (1999) **4.** Cohen, E. *et al.*, NeuroImage 23: 613 (2004) **5.** Yablonskiy, D. and Haacke, E., Magn. Res. Med. 32: 749 (1994)

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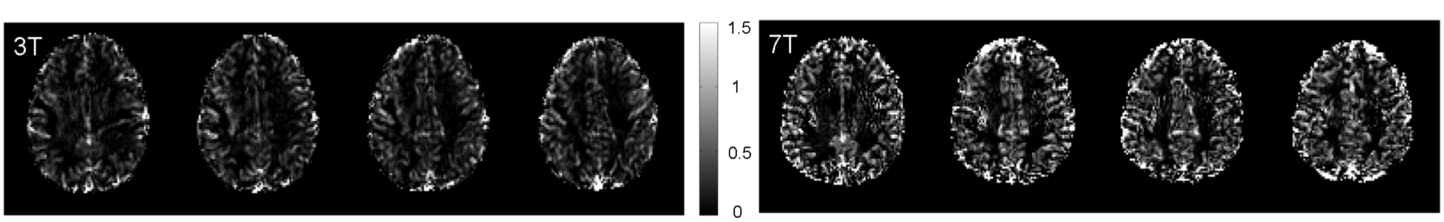

Figure 3: CVR maps of the same subject at 3 and 7T. The scale ranges from 0 to 1.5 %.