

Evaluation of a multiparametric qBOLD (mqBOLD) and cerebrovascular reserve in patients with severe intracranial arterial stenosis : a comparison study

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Introduction

To identify hemodynamic alteration related to steno-occlusive disease, functional MRI of cerebrovascular reserve (CVR fMRI) to hypercapnia has been proposed. A decreased vascular reserve downstream a severe intracranial arterial stenosis (SIAS) was associated with increased apparent diffusion coefficient, suggesting a chronic low-grade ischemia [1]. However, relationships between hemodynamic disorder and metabolism has not been shown using MRI, yet. In such patients, these abnormalities may further motivate endovascular stenting [2]. The aim of this study was to determine the relationships between tissular oxygen metabolism assessed with a multiparametric qBOLD (mqBOLD) approach with basal and functional changes of perfusion in patients with SIAS.

Materials and Methods

Groups. Twelve subjects (10 males/2 females range from 28 to 85 years ($m \pm sd 64.6 \pm 14.9$ yo)) with severe intracranial arterial stenosis located on the right ($n=8$) or left ($n=4$) internal carotid (ICA) ($n=5$) or middle cerebral artery (MCA) ($n=7$) were included in this study.

Acquisition. The imaging protocol was carried out on a 3T TX Achieva MR scanner (Philips Healthcare®) using a whole-body RF transmit and 8-channel head receive coils. Three sequences were acquired with a FOV of 224x20x184mm: a 3D multi gradient echo (GE) sequence to obtain a T_2^* estimate; a multiple spin-echo experiment for T_2 mapping; a perfusion sequence with injection of a bolus of Gadolinium-DOTA (0.1mmol/kg, Guerbet, France) to map cerebral blood volume (CBV) cerebral blood flow (CBF) and mean transit time (MTT). BOLD CVR fMRI was acquired with a block-design hypercapnic challenge (8% CO_2). Average end-tidal CO_2 pressure (Et CO_2) was used as a physiological regressor for statistical analyses with a general linear model (SPM8) [2]. After normalization, the final spatial resolution was 2*2*2mm.

Data Analysis. As described in the literature [3], St O_2 maps were obtained pixelwise from a combination of CBV and T_2' where $1/T_2' = 1/T_2^* - 1/T_2$ and using a haematocrit of 0.4. A map of Cerebral Metabolic Rate of oxygen (CMRO₂) was computed using $CMRO_2 \approx CBF \times (1 - StO_2/100)$. Regions of interest (ROI) measures on both %BOLD signal change/mmHg Et CO_2 and CMRO₂ were delineated on segmented gray matter of the MCA territories. We calculated a laterality index with $LI_{MCA} = (Left_CVR_{MCA} - Right_CVR_{MCA}) / (Left_CVR_{MCA} + Right_CVR_{MCA})$. Correlations across parameters and linear regression study to determine which parameters may predict CMRO₂ were computed using SPSS.

Results

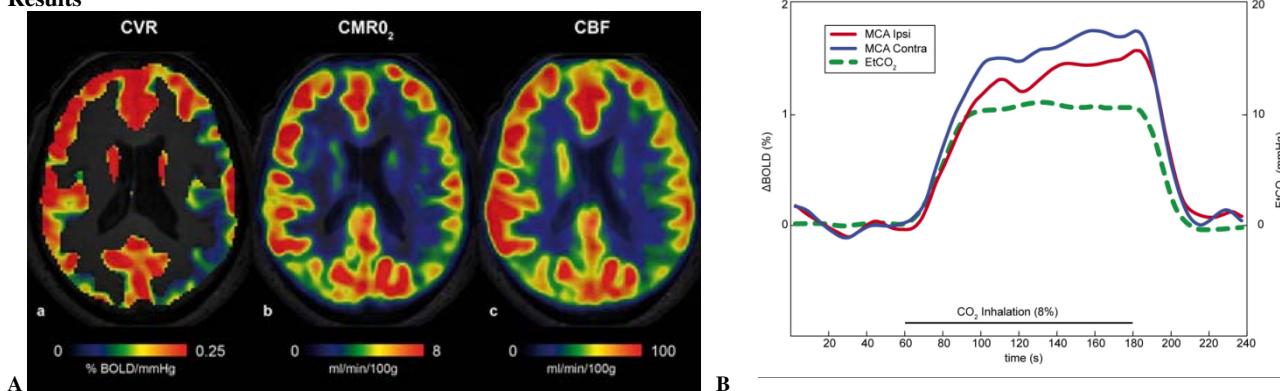


Figure 1 A. Illustrative individual maps, representing BOLD response to hypercapnia showed an alteration of the CVR which was accompanied by both decreased CMRO₂ and CBF (a-c). **Figure 1 B.** Regressor used for fMRI analyses based on mean Et CO_2 variation time courses during hypercapnia (green line). Percentage of BOLD signal averaged over three blocks. Amplitudes of both MCA territories were represented (red and blue lines). The amplitude decreased in the ipsilateral MCA territory relative to the contralateral MCA territory.

Our method provides parametric maps with sufficient spatial resolution to show an alteration of CVR and CMRO₂ and to distinguish regional differences in the contralateral hemisphere (Fig 1 A). Fig 1 B. represents BOLD signal curves obtained after normalization for the Et CO_2 time lag and regressor used for fMRI analyses based on mean Et CO_2 variation time courses during hypercapnia.

Perfusion: in the MCA territory ipsilateral to SIAS, CBF and Tmax values were 65.2 ± 27.2 ml/100g/min and 2.7 ± 0.9 sec, respectively. In the contralateral MCA territory, these parameters were 76.6 ± 34.5 ml/100g/min and 2.3 ± 0.8 sec. For CBF, Tmax, paired Student's t tests showed significant differences between ipsi- and contralateral MCA territories. LI_{MCA_CBF} ranged from -0.16 to 0.13.

CVR: paired Student's comparisons showed that mean CVR values were significantly lower in the ipsilateral MCA territory (0.18 ± 0.07 %BOLD/mmHg) than in the contralateral hemisphere (0.21 ± 0.08 %BOLD/mmHg). LI_{MCA_CVR} ranged from -0.27 to 0.14.

Oxygenation : mean CMRO₂ values measured in the ipsilateral MCA territory (4.6 ± 1.8 ml/100g/min) were significantly lower than CMRO₂ measured in the contralateral MCA territory (5.3 ± 2.2 ml/100g/min) ($p < 0.001$). For mean St O_2 values, no significant difference was observed between the ipsilateral MCA territory ($45.2 \pm 5.1\%$) and the contralateral territory ($46.4 \pm 5.4\%$). $LI_{MCA_CMRO_2}$ ranged from -0.18 to 0.11.

Correlations and regression: among interhemispheric differences estimated by laterality indices, significant correlations were detected between $LI_{MCA_CMRO_2}$ and: LI_{MCA_CBF} ($R = 0.93$; $p < 0.001$); and LI_{MCA_CVR} ($R = 0.92$; $p < 0.001$); and LI_{MCA_MTT} ($R = -0.68$ $p < 0.02$). To explain $LI_{MCA_CMRO_2}$ step by step linear regression selected LI_{MCA_CBF} and LI_{MCA_CVR} as significant $LI_{MCA_CMRO_2}$ among all perfusion parameters and CVR. Indeed, LI_{MCA_CBF} and LI_{MCA_CVR} accounted for 54% and 46% of the $LI_{MCA_CMRO_2}$ variance.

Discussion / Conclusion

This study is the first report of oxygenation mapping obtained with MRI on patients with SIAS. The impairments of basal and functional changes of perfusion predicted oxygenation decrease, suggesting low-grade ischemia in the parenchyma downstream SIAS. The mqBOLD method provided high resolution maps in patients with SIAS and may be a promising complementary MR technique in the management of patients with hemodynamic disorder.

References

[1] Conklin et al. Neurology 2011. [2] Attye A et al. HBM 2013. [3] Christen T et al. NMR in biomed 2011.