Quantification of Cerebrovascular Reactivity by BOLD MRI and Correlation with Conventional Angiography in Patients with Moyamoya Disease

C. Heyn[1], J. Poublanc[1], J. S. Han[2], D. M. Mandell[1], J. A. Stainsby[3], A. P. Crawley[1], K. G. terBrugge[1], J. A. Fisher[2], and D. J. Mikulis[1]

[1]Medical Imaging, Toronto Western Hospital, Toronto, Ontario, Canada, [2]Anesthesia, Toronto General Hospital, Toronto, Ontario, Canada, [3]Diagnostic Imaging, GE Healthcare, Toronto, Ontario, Canada

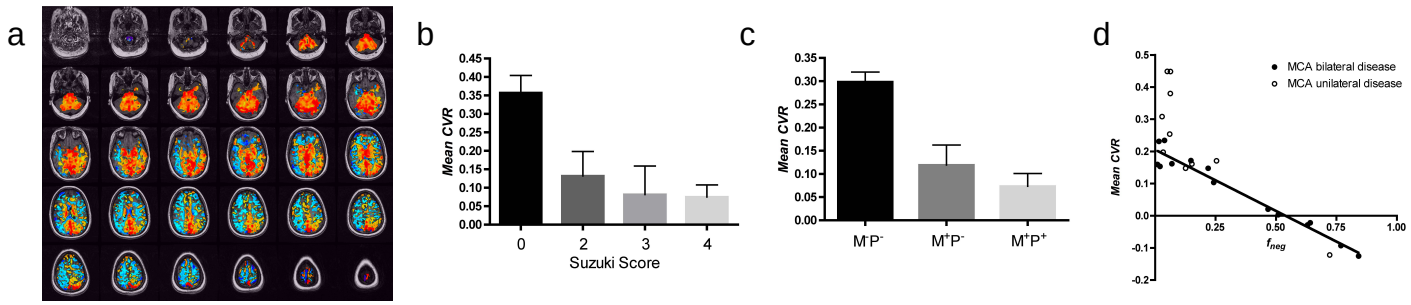
Introduction

Moyamoya disease (MMD) is a vasculopathy characterized by progressive narrowing of proximal circle of Willis vessels and the formation of secondary collaterals. Blood flow distal to these stenotic vessels is thought to be maintained by a drop in vascular resistance mediated by small artery and arteriolar vasodilatation. As the disease advances, the ability of this autoregulatory system to preserve adequate perfusion is lost when compensatory vasodilatation reaches a maximum. Further increases in vascular resistance ultimately leads to tissue oligemia and possible ischemia. In patients with MMD, cerebrovascular autoregulation can be assessed by measuring the effect of PCO_2, a vasodilator, on cerebrovascular blood flow. A number of techniques exist for this including perfusion imaging with SPECT, PET, and transcranial doppler (TCD) under conditions of high PCO_2 or acetazolamide stress. Recently, we have developed a methodology for rapidly and accurately controlling end tidal PCO_2 utilizing a CO_2 rebreathing device. Using this technique with blood oxygen level dependent (BOLD) MRI, a quantitative map of cerebrovascular reactivity (CVR), defined as the change in MR signal per mmHg change in end tidal PCO_2, can be generated for patients with MMD. The advantage of this methodology is that it has high spatial resolution compared to other imaging modalities, and is quantitative unlike methods which cannot precisely control end tidal PCO_2. In the present work, we apply BOLD CVR to patients with MMD and correlate the quantitative high resolution maps with angiographic features found on conventional vessel angiography.

Methods

Patient Selection: A retrospective analysis was performed on patients with MMD who underwent BOLD CVR studies at our institution prior to surgical revascularization. All patients had a six vessel conventional angiography performed within 6 months of the CVR study. Patients with ischemic or hemorrhagic infarcts were excluded from the study. ***MRI:*** MRI was performed on a 3.0 T GE clinical MRI scanner equipped with 40 mT/m gradient coils and an 8 channel head coil. A standard single-shot BOLD protocol with a spiral read out (TE 30 ms) was employed. The imaging time was 12 minutes for a total of acquisition of 320 volumes. Each volume contained 28 slices with a resolution of 3.75×3.75×4.5 mm. PCO_2 was tightly controlled using a rebreathing circuit. The technique results in a near square wave change in PCO_2 with a constant elevated plateau of 45 to 50 mmHg and rapid transition from low to high PCO_2 within 5 breaths. ***Data Analysis:*** AFNI was used to fit the BOLD signal to the PCO_2 reference waveform and to transform to Talairach space. Vascular territories defined by templates were used to calculate mean CVR in each territory. CVR for each voxel was calculated from the MR signal difference (ΔS) and the change in end-tidal CO_2 (ΔPCO_2): $CVR_{voxel} = \Delta S/\Delta PCO_2$ [Eq. 1]. The mean CVR for 6 vascular territories was calculated as a weighted average of voxels with positive CVR (CVR_{pos}) and negative CVR (CVR_{neg}): $mean\ CVR = f_{neg} \bullet CVR_{neg} + f_{pos} \bullet CVR_{pos}$ [Eq. 2]. f_{neg} and f_{pos} are the fraction of negative and positively reacting voxels respectively. Negatively reacting voxels occur as a result of vascular steal phenomenon. Equation 2 can be re-expressed: $mean\ CVR = -(CVR_{pos}\text{-}CVR_{neg}) \bullet f_{neg} + CVR_{pos}$ [Eq. 3]. ***Angiography:*** Conventional angiography was read by a neuroradiologist. The presence of moyamoya or pial collaterals in each vascular territory and the degree of MMD staged using a modified Suzuki score (Mugikura et. al, Stroke 2002;33;1497-1500) was recorded for each patient.

Results



Twelve patients with MMD, age 10 to 48 years, were included in the study (7 females, 5 males, mean age 35.2 years). (a) CVR map is shown from one of the cases. Areas of red/orange indicate positive reactivity whereas blue areas correspond to negative reactivity. (b) The mean CVR in the MCA territory is plotted against the Suzuki score. There is a trend to decreasing reactivity with increasing disease severity (increasing Suzuki score). A significant difference in mean CVR for patients with a Suzuki score of 0 and Suzuki scores of 2,3, and 4 ($p<0.05$) was found. (c) Vascular territories with moyamoya (M+P-) or moyamoya and pial (M+P+) collaterals had significantly lower mean CVR compared to territories without disease ($p<0.05$). There was a trend to decreasing mean CVR for vascular territories with moyamoya and pial collaterals versus moyamoya collaterals alone but the difference was not statistically significant. (d) Mean CVR was plotted against the fraction of negatively reacting voxels (f_{neg}) for all MCA territories. The solid circles represent patients with bilateral MMD and open circles correspond to patients with unilateral disease. A linear regression was fitted for patients with bilateral disease (slope=-0.38, y-intercept=0.21)

Discussion

Reduction in mean CVR correlates well with the degree of MMD disease measured by modified Suzuki score or the presence of moya vessels and pial collaterals as visualized by conventional angiography. For patients with bilateral MMD, there is a linear relationship between mean CVR and f_{neg}. The relationship follows Equation 3, with the y-intercept corresponding to CVR_{pos} and the slope $-(CVR_{pos}\text{-}CVR_{neg})$. The implication of this linear relationship is that for patients with bilateral MMD, there is a minimum value for mean CVR for all positively reacting voxels defined by the y-intercept (0.21) and a constant value for mean CVR for all negative reacting voxels (-0.17). According to this analysis, the main factor leading to reductions in mean CVR for a given vascular territory is the increase in the extent of voxels with negative reactivity (f_{neg}). In other words, as disease severity increases, reduction in mean vascular reactivity results from an increase in the volume of brain experiencing vascular steal rather than a decrease in mean reactivity for negatively reacting voxels which remains constant. The current study demonstrates how BOLD MRI combined with methodology for tightly controlling end-tidal PCO_2 can provide high spatial resolution maps of vascular reactivity in patients with MMD. CVR maps correlate well with angiographic features of MMD and provide quantitative information on the severity of disease.