

Feasibility of non-invasive quantitative MRI measurements of cerebral vascular reactivity using a computer controlled stimulus in children with sickle cell disease

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Introduction: Sickle cell disease (SCD) is the major cause of stroke in children leading to mortality or long-term disability [1]. A noninvasive means of measuring cerebral blood flow (CBF) reserve would facilitate assessment and clinical management of these patients [2]. Cerebrovascular reactivity (CVR), an indirect measure of CBF reserve, is defined as the CBF response to a vasodilatory stimulus. BOLD MRI has been used as a surrogate for CBF changes in response to a vasoactive stimulus such as partial pressure of CO₂ (PCO₂). The recent introduction of precise control of end-tidal PCO₂ (PETCO₂) and PO₂ (PETO₂) via a computer-controlled, model-driven prospective end-tidal targeting (MPET) system [3] has improved the reliability of BOLD based CVR measures in healthy and diseased adults. However, within the pediatric population, CVR studies are not common. Therefore the aim of this study was to 1) introduce this technique to a pediatric population with SCD, 2) demonstrate the type of information that can be derived; and 3) discuss advantages and disadvantages over existing CVR methods. For this purpose we report our experience with CVR studies in 11 pediatric SCD patients.

Materials & Methods: 11 SCD patients (7-18 years) were imaged on a 1.5T MRI system (GE Healthcare, Milwaukee, WI). PCO₂ and O₂ targets were achieved using an MPET system with a custom built breathing circuit (RespirAct, Thornhill Research Inc., Toronto, ON). MR imaging was performed in synchrony with the MPET using a standard BOLD sequence (TE = 40 ms, TR = 2 s, FOV = 220 mm, matrix size = 64×64, slices = 25, slice thickness = 4.5 mm, volumes = 240, scan time = 8 min). BOLD images were analyzed offline using FSL. The data was assessed by correlating the BOLD signal change in time with the measured end-tidal CO₂ values of each subject, and then normalizing over the mean signal to produce a voxel-wise map of CVR. Imaging also included anatomical imaging as well as MR angiography. Structural MRI, MRA and CVR maps were assessed visually by an experienced neuroradiologist (MS) as well as an imaging scientist (AK).

Results: There was a strong concordance between CVR and angiographic findings. Five patients had angiographic abnormalities and also had reduced overall CVR. Three out of these exhibited steal effect in the corresponding parenchymal territories. The six patients who had a normal angiogram also revealed lower CVR compared to healthy individuals, but was generally less severe than those with angiographic abnormalities. All patients in this study had ischemic changes in the brain parenchyma as identified with structural MR imaging. Nine of the 11 patients demonstrated mapped reductions in CVR extending beyond the ischemic lesions (as identified with MR structural imaging) into normal appearing brain parenchyma. Example cases are shown in Figure 1.

Conclusion: The combined application of tightly controlled reproducible changes in PCO₂ and BOLD MRI for generating whole brain maps of CVR is a promising method for imaging the distribution of vasodilatory reserve in children with SCD. No complications of the procedure were encountered in this observational study, matching our experience in over 150 examinations in adults. In our small cohort of 11 patients, CVR provided information on the severity and distribution of hemodynamic compromise that could not be obtained from traditional clinical assessment and structural imaging. Further studies will be required to assess the reliability of this information for clinical management.

References: [1] Ganesan V et al. Ann Neurology 2003, 53:167-73, [2] Mandell D et al. Stroke 2008, 39:2221-8, [3] Slessarev M et al. J Physiology 2007, 581:1207-19.

Fig. 1: SCD case with normal angiogram (a) vs SCD case with abnormal angiogram (b) and corresponding CVR maps in relation to a healthy control (c)

