Assessment of cerebral perfusion and oxygenation in sickle cell disease using arterial spin labeling and BOLD MRI

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Introduction: Neurological complications such as stroke are well known consequences of sickle cell anemia (SCA). To date, high blood velocities recorded by transcranial Doppler (TCD) have been a useful indicator of stroke risk in children (2) however TCD is difficult to apply reliably in adult populations and does not give a measure of microvascular status. In a recent study of cerebral perfusion in SCA, Kirkham et al used dynamic susceptibility contrast to demonstrate regional reductions in cerebral blood flow and mean transit time in adult patients that correlated with neurological symptoms better than large vessel velocity measurements. While dynamic susceptibility contrast has been used for measuring blood flow and blood volume in SCD (1,3), it is often difficult to quantify across subjects and is not amenable to routine monitoring in sickle cell patients. We propose to use non-invasive arterial spin labeling perfusion MRI to determine cerebral blood flow (CBF) in an uncomplicated group of adult sickle cell patients. In addition we shall use BOLD MRI to determine the response to hyperoxia in SCA patients as a measure of cerebral deoxyhemoglobin concentration (4,5).

Subjects: MRI measurements were performed on 10 adult sickle cell patients (5 female 5 male, age 34+/- 9 range 23-53) and 16 control subjects (9 female,7 male, age 31+/- 7 range 22-48). Hematology examinations were done on all SCA patients as part of their normal clinical care. SCA patients underwent a brief neurological evaluation including assessment of reflexes, cranial nerves and neuropsychological testing (Forcheberg mini mental examination).

MRI: Imaging was performed on a 4 Tesla MR imaging system (Varian Inova). Quantitative ASL perfusion was measured using the FAIR technique in conjunction with single shot echo planar readout with in-plane saturation (TI=1.8s, TR=4s, res=64x64, FOV=19.2cm, slice thickness = 4mm). Perfusion slices were positioned approximately 3cm superior to the AC-PC plane. For hyperoxia response, 18 sequential spin echo images were acquired (9 transverse slices spaning 5 cm superior to the AC-PC line, res=64x64, TR=1.2sec, TE=50msec, FOV=19.2cm, slice thickness = 5mm) while the breathing gas was cycled from air to pure oxygen and back to air (4,5).

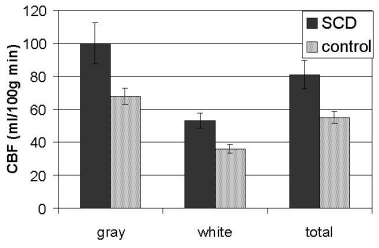

Figure 1: Average perfusion in gray matter, white matter, and whole brain in SCA patients and control subjects.

Results: Figure 1 shows the group averaged CBF in the control and sickle cell subjects. In general we found that CBF was approximately 45% higher in the SCA subjects in both gray matter and white matter. This is consistent with autoregulatory compensation for systemic anemia (mean hematocrit = 26+10). CBF in SCA decreased with age and hematocrit, which agrees with previous results using xenon washout (6). CBF was also inversely correlated with red cell distribution width (RDW) in the SCA patients. Increased RDW can be a surrogate for increased red cell density that is an important factor in hemoglobin polymerization. Multi parametric fitting, accounting for both age and hematocrit, revealed that 2 of the 10 subjects had lower cerebral perfusion than predicted for their age and hematocrit (although the perfusion values were comparable to those in control subjects). One case of hypoperfusion corresponded to the only subject with poor performance on neurological examination. The average BOLD hyperoxia response was approximately 4 times greater in SCA patients than in controls. The increased BOLD response indicates higher levels of cerebral deoxyhemoglobin under ambient conditions that are preferentially alleviated in SCA patients under hyperoxia(5). Higher levels of deoxyhemoglobin can increase the probability for further polymerization and vaso-occlusion. These studies are the first to establish quantitative CBF levels in uncomplicated adult SCD patients using ASL and will enable further studies in higher risk populations such as children. While there are many factors that can influence cerebrovascular function in SCD, the unique non-invasive capabilities of quantitative MRI can be an important tool in the understanding and management of this disease.

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