Perfusion asymmetries and flow in children with Sickle Cell Disease assessed by pseudo-continuous Arterial Spin Labeling and Phase Contrast MRI

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Introduction
Sickle cell disease (SCD) is a hereditary anaemia characterized by chronic haemolytic anaemia and vascular occlusion. One of the complications of SCD is cerebral infarction, present on MRI in one third of patients at the age of 18. Infarction diagnosed on MRI is not always accompanied by neurological deficit, but may be associated with decreased neurocognitive functioning and increased risk of new infarcts. Previously, arterial spin labeling (ASL) studies in SCD have shown perfusion asymmetries [1-3]. These asymmetries could be precursors of future (silent) infarcts and neurological deficits. However, it remains to be investigated whether these asymmetries are reflecting perfusion differences or if they result from technical difficulties encountered in ASL e.g. variations in labeling efficiency or insufficient delay time before acquisition. In this study we used pseudo-continuous ASL (p-CASL) [4] with two delay times and phase contrast MRI (PC-MRI) for flow measurements to further evaluate the origin of perfusion asymmetries in SCD patients.

Methods
Local ethics committees approved the study protocol. After written informed consent, nine consecutive SCD patients (aged 8 to 20 years) were included in this study. MR imaging was performed on a Philips 3T MR system using a SENSE-8-channel head coil and body coil transmission. Besides MR angiography and T2/FLAIR for clinical purposes, the imaging protocol consisted of: p-CASL, selective ASL by vessel-encoded p-CASL [5] and PC-MRI. Imaging parameters for p-CASL based sequences were: TR/TE 4000/14 ms; FOV 240×240; matrix size 50×79; slices 17; slice thickness 7 mm; no slice gap; single shot EPI, labeling duration 1650; post labeling delay 1500 or 2100 ms; background suppression; number of dynamics 80 (75 for selective ASL). In vessel-encoded p-CASL, selective labeling was accomplished by spatial manipulation of the labeling efficiency within the labeling plane in sets of 5 dynamics. Flow territories of the right internal carotid artery (R-ICA), the left internal carotid artery (L-ICA) and the basilar artery (BA) were determined by averaging dynamic scans with equal spatial encoding of labeling, resulting in one control, one globally labeled and three selectively labeled perfusion images. Procedures outlined by Wong et al. [2] were followed to calculate relative labeling efficiencies of the spatially manipulated scans. Flow territories were identified by means of k-means clustering. Perfusion weighted images and flow territories, were coregistered. After segmentation of perfusion weighted images into flow territories, cerebral blood flow (CBF) was quantified for all flow territories. Retrospectively gated (2 cardiac phases) PC-MRI [6] measurement was performed at a resolution of 0.5x0.5x0.5 mm3; TE/TR = 3.4/6.8 ms; flip angle: 15°; velocity encoding: 100x100x100 cm/s in the x, y and z direction respectively. GT-flow (provided by Gyrotools) was used to assess flow in semi-automatically defined ROIs placed in the BA and both ICAs just below the circle of Willis. Perfusion and flow asymmetry were assessed by calculation of the ratio between R-ICA and L-ICA CBF/flow. The correlation between CBF (delay 2100ms and 1500ms) and flow corrected for the volume of the flow territory supplied, was assessed, using Spearman's rho non-parametric test (with P-values <0.05 regarded significant (SPSS statistics 16.02)).

Results
Results on perfusion and flow measurements are shown in Table 1. In three out of nine patients perfusion asymmetries were observed at a delay of 1500 ms, with ICA perfusion ratios of 0.9, 1.1 and 0.7 respectively (mean of other patient data was 1.0 with values ranging from 0.96-1.04). In two of these patients asymmetries resolved at the longer delay time of 2100 ms before image acquisition; in one patient, asymmetries persisted. In all three patients asymmetries were also observed in flow measures and in flow corrected for the volume of the flow territory supplied. Perfusion weighted images and flow territories of two patients with perfusion asymmetries, are shown in Figure 1. No significant correlation was found between CBF (delay 2100ms) and flow corrected for volume of the corresponding flow territory (correlation coefficient 0.34, P=0.07) (data of all patients included). The correlation coefficient for the correlation between CBF (delay 1500ms) and corrected flow was 0.27 (P=0.19).

Discussion
The results of this study indicate that CBF asymmetries can resolve with sufficient delay times, as was seen in two out of three patients. Wang et al. [7] showed that, after a delay of 1500 ms, most of the spins in grey matter are in the tissue compartment and in healthy volunteers, delay time dependent asymmetries should thus have disappeared by then. In previous ASL studies [1-3] that have shown perfusion asymmetries in SCD patients, data were gathered with shorter delay times. Only in one patient the asymmetry remains with a longer delay time. In this patient the asymmetry was also observed in flow of the ICAs. In case of an anomaly of the circle of Willis, flow asymmetries might not be compensated for. Consulting MRA data however, showed that this patient did have a complete circle of Willis allowing for redistribution of flow. Possibly flow velocity in the ICAs of this patient influenced labelling efficiency. The correlation coefficient (0.34) indicates that there is at least a trend towards a positive correlation between flow corrected for the supplied volume and CBF in the supplied flow territory. The latter suggest that flow is an important determinant of the perfusion measured by ASL in this population.

References