Non-invasive perfusion measurements in term neonates and premature infants at term-equivalent age using arterial spin labelling

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Introduction

Sick premature and term neonates have a vulnerable cerebral circulation [1]. Impaired autoregulation of the cerebral blood flow and thus cerebral perfusion is probably one of the main contributors to the development of brain damage in these infants [2,3]. Studies of the cerebral circulation have been performed previously using different invasive methods such as xenon-clearance, PET and SPECT [1,4,5]. Non-invasive approaches for estimating CBF, e.g. Doppler ultrasonography and near infrared spectroscopy (NIRS) [6] have not accomplished the primary expectations [7]. However, a non-invasive MR method for accurately measuring brain perfusion has recently been developed. Arterial spin labelling (ASL) is a MR technique that enables accurate maps of regional cerebral perfusion to be acquired in a few minutes. As this MR method is entirely non-invasive and safe, even in very young infants, the measurements may be repeated. This approach will therefore facilitate investigations into the underlying pathogenetical mechanisms of brain damage in high-risk neonates.

Purpose

The purpose of this study was to investigate the feasibility of ASL as a method for measuring cerebral perfusion in healthy premature infants at term equivalent age and in term neonates.

Subjects and methods

20 infants were enrolled in this prospective study. Nine infants were born prematurely (group 1) at a median gestational age (GA) of 31 weeks (30-34), with a median postmenstrual age (PMA) of 40 weeks (38-41) at the time of MR examination. Eleven infants were healthy term neonates (group 2) born by elective and uneventful caesarean section at a median GA of 39 weeks (38-39), median PMA at the time of MR 39 weeks (38-40). Consequently infants in both groups had similar developmental ages. Apgar scores and umbilical cord pHs were normal for all infants. The premature infants were clinically stable throughout the neonatal period and had normal brain ultrasound scans. The local ethics Committee accepted the study and informed parental consent was obtained in all cases. For the MR examination infants were unsedated, sleeping naturally after a feed and wrapped in blankets and a slightly deflated vacuum pillow. Padded silicone ear cups were used for noise protection. All images were acquired on a Siemens Magnetom Trio 3T scanner using a PICORE QUIPSS II sequence [8] with the following parameters: 16-20x5mm slices, 0.5mm slice gaps, TI_1/TI_2/TE/TR=700/1500/23/2700ms, FOV=192mm, 64x64 matrix EPI readout, 124-140 repetitions. The images were aligned using the SPM2 realignment tool [9]. The realignment curves were inspected visually and motion-free periods were identified. Control and tag images acquired during the motion-free periods were subtracted to give perfusion-weighted ASL images. Regions of interest (ROIs) were drawn on the control images in the basal ganglia (BG), cortical grey matter (GM) and white matter (WM). Mean perfusion values were calculated for each ROI and each subject. T_1 of blood was assumed to be 1.5s for perfusion quantification.

Results

Three subjects were excluded due to excessive motion (2 from gr.1 and 1 from gr. 2). For the remaining subjects, 70-140 images were found to be motion-free and thus contributed to the ASL images. Results are shown in table 1. Figure 1 shows an example of anatomical images and perfusion images in two axial slices in one subject. ASL was found to be a feasible method for measuring perfusion in neonates even when they are unsedated. Motion is a substantial problem but can be solved in most cases. Acquisition time is short (approximately 6 minutes). The calculated values correspond to values acquired using other methods. Perfusion is highest in BG and lowest in the WM.

We found higher perfusion values in the BG and GM for premature infants at term equivalent age as compared with term neonates. These differences were highly significant (p values .001 and .001, for BG and GM respectively). However, in the WM there were no significant differences in perfusion between groups due to the low SNR. No significant differences were found in the BG: GM and BG: WM perfusion ratios.

Conclusions:

ASL is feasible for measuring perfusion in neonates and the obtained perfusion values are reliable. Perfusion values in BG are much higher as compared with GM and especially WM. Values in WM are low. Values of perfusion in premature infants at term equivalent age are significantly higher than in term neonates. ASL, allowing serial perfusion measurements, offers the possibility of better understanding pathogenetical mechanisms underlying brain damage in high-risk neonates.

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	Median	Mean	SD
BG group1	19.4	20.2	5.4
BG group 2	12.1	11.8	2.5
WM group 1	2.7	3.8	2.9
WM group 2	2.5	1.9	2.6
GM group 1	7.5	8.8	2.7
GM group 2	4.3	3.6	2.4
WM1/ BG1	16%	18%	8%
WM2/ BG2	17%	14%	2.7%
GM1/ BG1	44%	44%	8%
GM2/ BG2	32%	29%	24%

Table 1:*Regional-perfusion values for basal ganglia (BG), white matter (WM) & cortical grey matter (GM), perfusion quantified in ml/ 100-g tissue/ minute (1-6 rows) and normalised data in relation to Basal ganglia values (7-10 rows). 1 = premature infants at term equivalent age, 2= term infants.*

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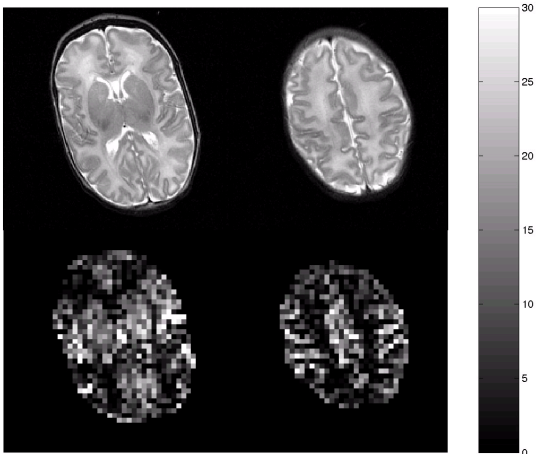

Figure 1: *T2 TSE images (upper) & perfusion images at the level of BG & CSO. Image intensities in the perfusion images (see colour bar) are perfusion in ml/100 g/ min.*

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