Assessing brain damage after perinatal hypoxic-ischaemia using an automated protocol for combined regional analysis of the Cerebral Blood Flow and MR spectroscopy

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MOTIVATION:

Perinatal hypoxia-ischemia (HI) can cause catastrophic alteration of brain metabolism and physiology [1], resulting in neonatal encephalopathy. Metabolic changes detected using magnetic resonance spectroscopy (MRS) have been used as a reliable predictor of clinical outcome [2]. Abnormalities in cerebral blood flow (CBF), reflecting cerebral physiology, have also been linked to HI [3]. The potential of combining these two MR biomarkers has been recently proposed [4] and shown to increase the predictive power of MRS in deep grey matter (DGM) [5]. The CBF analysis in [5] was limited to DGM; extending this analysis to other brain regions might provide further insights into different patterns and severity of the pathology resulting from HI. The aim of this study was to develop an automated framework for regional analysis of CBF and to investigate the added value of combining thalamic MRS with such detailed regional CBF analysis for the inclusion of ASL as a potential biomarker of outcome in HIE.

METHODS:

This study was approved by the local ethics committee. Fourteen term neonates (mean gestational age 39 weeks; 38-41+6 weeks) with neonatal encephalopathy were included. Written consent was obtained from the parents. All neonates underwent therapeutic hypothermia and were scanned between the 3rd and 7th day of life. In addition to the standard clinical brain imaging protocol (high resolution T1, T2 and diffusion-weighted imaging, and thalamic MRS), ASL and carotid phase contrast flow measurements (QFlow) were also acquired.

MRS: a water-suppressed PRESS sequence was positioned in the thalamus (64 averages, TR/TE = 2288/288ms, voxel size 15x15x15mm, ~7 min). Lactate to N-acetylaspartate (Lac/NAA) peak ratio was calculated after fitting using the AMARES algorithm (jMRUI). Subjects were divided into two groups based on Lac/NAA peak ratio: below 0.3 = unlikely unfavourable outcome (N=9) and above 0.3 = high risk of poor outcome.

ASL acquisition & processing: a pseudo-continuous ASL (pCASL [6]) was used with labeling duration of 1.7s, post-labeling delay of 1.5-2s, readout: GE-EPI with FOV 240x240mm^2, acq matrix 64x64 and TR/TE 4000/20ms, background suppression (11 neonates) (~8 min). Proton density (PD) images were acquired using the same readout with identical parameters. Before averaging, all raw ASL images were corrected for motion by registration to a subject-specific template (DTI-TK [7]) and by intensity-based automated identification and exclusion of corrupted data. CBF was quantified using the single compartment kinetic model [8]; T1 of the blood was calculated for each baby based on measured hematocrit (Htc) values according to equation: 1/1.Tb = 0.5*Htc +0.37 [9]. Labeling efficiency was set to 0.77, as estimated by numerical simulations of Bloch Equations for a velocity range based on the carotid QFlow measurements.

Regional CBF: regional CBF was calculated in Regions of Interest (ROIs) defined automatically based on both an atlas based probabilistic tissue segmentation of 5 tissue classes [10] and on a joint multi-atlas label propagation and fusion of 50 neonatal brain [11]. After affine and non-linear registration (Nifty-Reg [12]) of the T2-weighted atlas images to the T2-weighted image of each neonate, the probabilistic maps and parcellations were propagated to individual subject space. Probability maps were used to segment T2 images (Nifty-Seg [13]). Finally, T2-weighted subject images were co-registered to the CBF maps using rigid registration, with the tissue segmentations and brain parcellation propagated to CBF space. Grey matter (GM) and deep grey matter (DGM) CBF were quantified in the regions using tissue segmentations. Subsets of the parcellated areas were combined to create larger regions, corresponding to the main cerebral lobes (frontal, temporal, occipital, parietal) plus parasaggital cortex and insula. Left and right sides were added together to create a single mask. The ROIs were then used together with the GM mask to determine cortical regions. Similarly, the left and right parcellation of the deep grey matter nuclei (thalami, caudate and lentiform nuclei) were combined and CBF quantified using DGM segmentation as a mask. T-tests and F-tests were computed to investigate the statistical differences in mean and variance of CBF values between low- and high-risk groups.

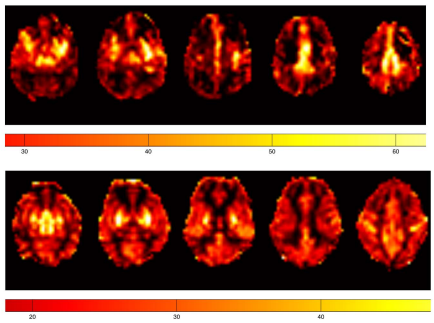

Figure 1. CBF maps of 2 neonates from the high risk group (thalamic Lac/NAA > 0.3)

RESULTS:

CBF maps were succesfully produced in all neonates. On average, 20% of motion corrupted data was rejected, leaving 36 control-label pairs per patient. Figure 1 shows an example of CBF maps of 2 neonates from the high-risk group with different degrees and patterns of brain injury. The results of the detailed analysis of regional CBF for neonates in low- and high-risk groups are shown in Figure 2. The boxes represent the 25th and 75th percentile, the band the median and the whiskers the spread of the data. In the low risk group, all CBF estimations are within a tight range for all brain regions (8-47ml/100g/min), whereas in the high-risk group, the range is much broader: (7-128ml/100g/min). In this group, the CBF of lentiform nuclei and parasaggital cortex have the most elevated values, as also seen in the CBF maps in Figure 1. There were statistical differences for CBF in the lentiform nuclei between the high- and low-risk groups (t-test, F-test <0.05) but not in the pasasaggital cortex (t-test=0.07, F-test < 0.05).

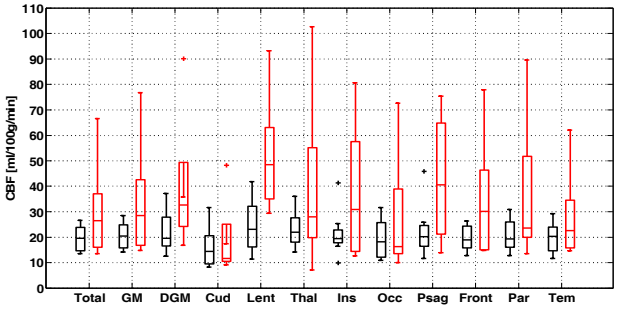

Figure 2. Results of detailed regional CBF analysis; neonates with thalamic Lac/NAA peak ratio below (black) and above (red) predictive value of 0.3

DISCUSSION & CONCLUSION:

This study presents a detailed analysis of regional CBF in conjunction with Lac/NAA peak ratio. ASL was used here as it provides a window to the physiology of the brain, over and above the information from structural, T1 /T2/diffusion weighted scans. Generally, an increase in CBF accompanies an increase in Lac/NAA, most notably within the DGM nuclei and parasaggital cortex. This increase in CBF could be related to the loss of autoregulation in severely affected babies, and this information has the possibility to further separate this group of patients from the moderately affected, usually evenly split by current imaging and clinical criteria between mild and severe HIE.

In addition, the proposed automated method of segmentation and parcellation increases the objectivity of ROI placement, making it user independent. It is less labour intensive and time consuming, and therefore more amenable for implementation in clinical practice. It is expected that long-term follow-up data of these neonates will enable correlation between CBF findings and clinical outcome.

REFERENCES

1. Pryds, O Annals of Neurology 30 (1991), 2.Thayyil S et al. Pediatr Res 125(2):382-95 (2010), 3.Pryds O et al. J Pediatr (1990),4. Sokolska M et al. Proc. Intl. Soc. Mag. Reson. Med. 22 (2014), 5. De Vis et al. Eur Radiol 0938-7994, (2014), 6. Dai et al. MRM 60:1488–1497 (2008), 7 Buxton RB et al. MRM (1998). 8.http://dti-tk.sourceforge.net 9.Varela et all. NMR Biomed (2011), 10. http://biomedic.doc.ic.ac.uk/brain-development/index.php?n=Main.Neonatal2. 11. http://biomedic.doc.ic.ac.uk/brain-development/index.php?n=Main.Neonatal3 12. http://sourceforge.net/projects/niftyreg/ 13. http://sourceforge.net/projects/niftyseg/