Differences in Blood Perfusion between Extremely Low Birth Weight (ELBW) Pre-term Infants and Control Term Infants

A. Caprihan[1], U. Sakoglu[1], J. Pfeuffer[2], J. Rael[3], J. Stephen[1], J. Lowe[3], S. Duvall[1], C. Gasparovic[1], R. K. Ohls[3], and J. P. Phillips[1,3]

[1]The Mind Research Network, Albuquerque, NM, United States, [2]Siemens Medical Solutions USA, Inc, Charlestown, MA, United States, [3]University of New Mexico, Albuquerque, NM, United States

Introduction

A considerable number of extremely low birth weight (ELBW) infants sustain a grade 3 or 4 intraventricular hemorrhage (IVH) resulting in a significant increase in the incidence of developmental delay and cerebral palsy. Reduced blood perfusion is one of the causes of ischemic brain injury. Although a variety of neuroprotective treatment strategies have been evaluated, no specific treatment has been identified to reduce or prevent brain injury. One potential new therapy is the use of human recombinant erythropoietin (Epo). In addition to stimulating erythropoiesis, Epo has been shown to be protective in the developing brain, making it possibly beneficial for very premature infants who are at risk for interventricular hemorrhage, hypoxic-ischemic injury, and developmental delay. We evaluated neurodevelopmental outcomes in preterm infants who received Epo during their hospitalization, compared to preterm infants who did not, and compared with healthy term controls. Previous studies have suggested that frontal lobe function is expected to be different in the ELBW children. In this study we compare blood perfusion measurements by pulsed arterial spin labeling (PASL) in ELBW children and healthy term controls. In addition, we report on the expected signal-to-noise ratio (SNR) for perfusion measurements in children by this technique for a 3T Siemens Trio Tim scanner.

Methods

Preterm infants ≤1500 grams birth weight who received at least 28 days of Epo were matched with infants who did not receive Epo, and with healthy term control infants. Follow-up data included anthropometric measurements, Bayley III scales of mental (MDI) and psychomotor (PDI) development, MRI scan, and neurologic exam. Data were collected at 18-22 months by certified examiners masked to the treatment group. Since this is a blind ongoing study, we are reporting only on differences between the ELBW and the normal control group.

Perfusion was measured by the standard FAIR-QUIPSII (1) arterial spin labeling (ASL) sequence on the 3T Trio Tim Siemens scanner. The pulse sequence parameters are: FOV = 220 mm, 64x64 matrix, 4 mm slice thickness with a 1mm gap, 24 slices are taken in the ascending order, TR = 4000ms and TE = 12ms. The pulse sequence consists of an interleaved global and slice-selective inversion recovery acquisition with a saturation pulse applied to a slab inferior to the imaging slices. The time delay between the inversion pulse and the saturation pulse TI1 = 700ms and the time delay between the inversion pulse and the excitation pulse TI2 = 1800 ms (1). We perform 105 scans, consisting of 52 pairs of control and tagged images. The total scan time is 7min. relCBF maps are calculated on the Siemens scanner based on the method described in (1). In addition we process the data off-line, which consists of a) image registration for motion correction, b) calculating the relCBF maps from the registered images, c) normalizing the relCBF maps to MNI space for group analysis, and calculating relCBF in user specified region-of-interest.

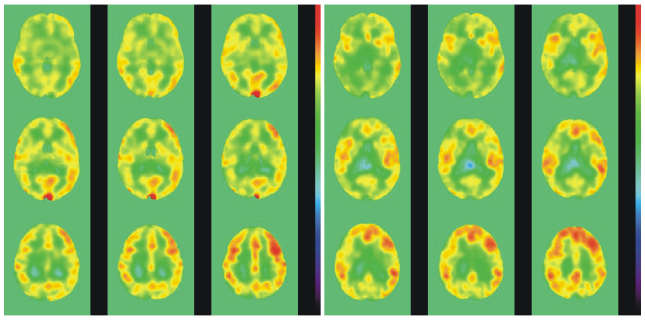
Results

a) relCBF (ml/100g tissue/min) was measured in five adults (25 – 60 years) and five infants (3 – 4 years). Mean flow and its standard deviation were calculated for the gray matter and the white matter. The mean flow in children was twice that in adults. The standard deviation of relCBF was slightly higher in gray matter for both the infants and adults. We give noise-to-signal ratio for the duration of the experiment and averaged over 25 voxels to indicate the amount of averaging required to get 5% measurement error. The NSR is higher in children because of their higher mean flows.

	relCBF	σ /voxel/experiment	NSR for 25 voxels
Gray matter (infants)	85	19.4	0.046
White matter (infants)	55	17.3	0.063
Gray matter (adults)	43	16.9	0.079
White matter (adults)	28	15.3	0.11

b) relCBF was measured in 12 ELBW infants. At present we cannot compare the effect of EPO because the study is blind and ongoing. The mean flow has ranged from 80 to 100 ml/100g tissue/min in gray matter and from 48 to 60 in the white matter.

c) The relCBF was compared in 2 ELBW infants and two age matched healthy control terms (18-22 months). The relCBF maps after normalization to the MNI space are shown on the right. The relCBF in healthy controls was on the average 15% higher in the gray matter. In addition there were regions in the frontal part of the brain where it was up to 20% higher. There was no difference in cognitive and the language test scores for these two groups of infants.



relCBF maps (ml/100g tissue/min)

Discussion

Fair-QUIPSII is a robust ASL method for measuring perfusion in children. On a 3T Siemens system we can get 5% error in gray matter with 7 min of experiment and averaging over 25 voxels. The perfusion measurement in ELBW children were 15-20% lower than the age-matched healthy term born infants. As the number of subjects increase we will be able to calculate the statistical significance of the observed differences.

References: 1. J. Wang et al. J Magn Reson Imaging 2003;18(4):404-413.

Acknowledgements: Supported by a grant from The Mind Research Network.