Non-invasive assessment of Cerebral Metabolic Rate of Oxygen in neonates.

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Introduction

Preterm birth has a worldwide incidence of 9.6%. Of these infants, 25-50 % develops cognitive deficits and 5-10 % motor deficits. White matter disease plays an important role here. Underlying pathogenic mechanisms are hypoxia-ischemia or hyperoxia. For optimal titration of oxygen supply, one should be able to measure Cerebral Metabolic Rate of Oxygen ($CMRO_2$). In addition, there may be a relation between $CMRO_2$ and tissue viability after an ischemic event such as perinatal arterial ischemic stroke or asphyxia. Positron Emssion Tomography (PET) has been used to evaluate $CMRO_2$ in neonates. However, the invasiveness of this approach urges the need for a non-invasive technique to assess $CMRO_2$. Recently, MR techniques have been developed which enable measurement of oxygen extraction fraction (OEF)[1,2]. Here we propose a combined approach of OEF-and perfusion measurements to obtain estimates of $CMRO_2$ non-invasively. The T2 Prepared Blood Relaxation Imaging with Inversion Recovery (T2-TRIR) sequence[2] was used to measure the OEF and brain perfusion was measured with Arterial Spin Labeling (ASL) MR imaging. Preliminary results are shown and compared to the existing literature. In addition, $CMRO_2$ was measured in infants diagnosed with asphyxia.

Materials & Methods

MR Imaging was performed in line with institutional guidelines (3T,Philips). Subject characteristics of the 11 included neonates are given in Table 1. Scan parameters of the pulsed ASL experiment were; matrix 40x40, FOV 240x240 mm, SENSE=2.5, voxel 3x3x6mm, gap 1mm, TR/TE/TI: 2500/20/1500ms, Q_2TIPS 600 ms and scan time 3:00. Scan parameters of the T_2-TRIR[2] sequence were: TR/TE/ΔTI/TI1= 1500/20/150/130ms, matrix 128x128, FOV 160x160, FA 95°, 2mm slice, SENSE=2.5, eTE=0,40,80 and 160ms and scan time 2:15. Perfusion was quantified on the ΔM images of the ASL scan[3]. The longitudinal relaxation rate of blood (T_{1b}) and the transverse relaxation rate of blood (T_{2b}) were fitted from the four inversion recovery curves obtained in the superior sagittal sinus with the T2-TRIR sequence, using the formula; $M_b(TI) = M_{ob}[1-(1.0 + e^{-eTE/T2b}.IE).e^{-TI/T1b}]$. From the T_{1b} the hematocrit (htc) was estimated; $1/T_{1b} = 0.50 .Htc + 0.37$[4]. Subsequently, venous oxygen saturation (Yv) was estimated from the T_{2b} and htc[5] (Figure 1). Arterial oxygen saturation (Ya) was measured using pulse oximetry. Finally, OEF and $CMRO_2$ were calculated: OEF= ((Ya-Yv)/Ya).100 and $CMRO_2$ = CBF (Ya-Yv) .Ca, with Ca = 1,89596 .0.1. Htc [6].

Figure 1

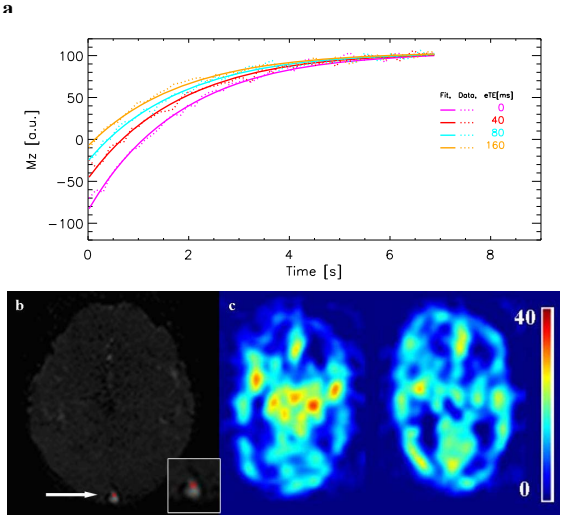

Figure 1. a) *Single voxel example fit to the four inversion recovery curves (eTE=0,40,80 and 160ms). Four different inversion recovery curves allow for robust fitting of T_1 and T_2.* ***(b)****. The surrounding tissue is saturated while only "fresh" blood is imaged. The sagittal sinus is automatically localized* ***(a,b)*** *The current fit results in a T1 of 1.85, T2 of 61.3ms. From this a Htc of 0.34 and venous oxygen saturation of 56.2% is derived. Resulting in an OEF of 42.7%.* ***(c)*** *Example ASL perfusion image of an infant imaged at term-equivalent age.*

Results

Subjects were divided into 3 categories, characteristics are shown in Table 1. For all categories mean cerebral blood flow (CBF), OEF and $CMRO_2$ are shown. Extracted oxygen fraction was on average lower in the asphyxiated infants compared to infants imaged at TEA. Cerebral blood flow in both groups was comparable, resulting in a lower oxygen metabolism in the infants diagnosed with asphyxia.

	N	Postconceptional age (in wks)	Corrected postconceptional age (in wks)	CBF (in ml/100g.min)	OEF (in%)	$CMRO_2$ (in µmol/100g.min)
Preterm	1	29	30	11	29	27
TEA	4	30 [28-33]	41 [40-41]	9 [3]	45 [3]	29 [10]
Asphyxia	6	38 [37-41]	39 [37-42]	9 [3]	32 [4]	22 [9]

Table 1: Subject characteristics are given; age when born is denoted as postconceptional age (mean [range]), age when MR imaging was performed is corrected postconceptional age (mean [range]). Cerebral blood flow (CBF), oxygen Extraction Fraction (OEF) and Cerebral Metabolic Rate of Oxygen ($CMRO_2$) are given (mean [standard deviation]) for one infant scanned at preterm age, infants scanned at term-equivalent age (TEA) and for infants diagnosed with asphyxia.

Discussion

A non-invasive approach to measure hemodynamic parameters and in particular $CMRO_2$ in a vulnerable patient population is presented. Cerebral blood flow in neonates has earlier been shown to be low, our results obtained with ASL MR imaging are in line with this. In addition, OEF seems to be realistic. In the past, $CMRO_2$ in neonates has been measured with PET. Values ranging from 2,7 to 24 µmol/100g.min in preterm infants and 0 to 58 µmol/100g.min in infants imaged at term age were shown[7]. Our values are in the higher end of these ranges. Recently, Lu H et al presented another non-invasive approach to measure $CMRO_2$[8]. In their work, TRUST MRI[1] estimates of OEF were combined with perfusion estimates based on volume-flow measurements obtained with phase-contrast MR angiography. A mean $CMRO_2$ of 18,4 µmol/100g.min was measured. We seem to find higher $CMRO_2$ values although we have to point out that our study population is rather small. Interestingly, in our results we find lower oxygen metabolism in asphyxiated infants which opens the door to implementation of this approach in clinical studies.

Conclusion

Non-invasive assessment of $CMRO_2$ in neonates may yield important clinical information especially in neonates with asphyxia or stroke.

Acknowledgements

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References

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