

Abstract O-055 Table 1 Results of receiver operating characteristics analysis to estimate outcome with FA in WM and MD in thalami and cortex. SE—standard error, CI—confidence intervals

	AUC	SE	Significance	95% CI
White matter FA	0.859	0.057	0.000	0.747-0.970
Thalami MD	0.775	0.077	0.003	0.625-0.926
Cortex MD	0.803	0.069	0.001	0.667-0.939

have an unfavourable outcome. Cortical, thalamic and WM tissue labels were generated by neonatal atlas-based automated segmentation of the T2-weighted images [1]. Tissue labels were propagated onto the diffusion maps. FA and MD values were determined. Linear regression was performed to assess the correlation between FA/MD and DQ. Estimation of unfavourable outcome with FA/MD in WM and GM was examined using receiver operating characteristic (ROC) analysis.

Results Following correction for multiple comparisons and age at scan significant correlation was found between DQ and FA in WM ($p = 0.0002$), and MD in thalami ($p = 0.0002$) and cortex ($p = 0.005$). ROC analysis to estimate unfavourable outcome showed larger area under the curve (AUC) for FA in WM, than MD in GM (Figure and Table).

Conclusion These data show that FA in WM and MD in GM may be used as biomarkers of outcome following HIE.

REFERENCES

1 Makropoulos *et al.* 2013

O-056

DOCOSAHEXANOIC ACID (DHA) GIVEN AFTER NEONATAL HYPOXIA-ISCHEMIA ATTENUATES LIPID PEROXIDATION AND BRAIN DAMAGE IN BOTH CORTICAL- AND WHITE MATTER TISSUES

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Background and aims Docosahexanoic acid (DHA) is a major component of membrane phospholipids and critical for fetal neuro-development. It accumulates during late pregnancy and may protect against oxidative damage to biomembranes. Isoprostanes, neuroprostanes, and neurofurans have all become attractive biomarkers of oxidative damage and lipid peroxidation in brain tissues. Lately also F₂-dihomo-isoprostanes have emerged as an *in vivo* biomarker of free radical damage to myelin in white matter.

Methods Global hypoxia was induced in newborn piglets (age 12–36 h) until Base Excess -20 mmol/L or mean arterial blood pressure <20 mmHg. One group ($n = 11$) was resuscitated with ambient air and another ($n = 10$) received in addition DHA 5 mg/kg 4 h after start of resuscitation. The piglets were followed for 9½ h after end of hypoxia.

Results Treatment with 5 mg/kg DHA 4 h after severe hypoxia significantly attenuated lipid peroxidation in tissues from cortex and hippocampus. There were less Isoprostanes in cortex and hippocampus in compared with reoxygenation with air (21%) alone, $p = 0.041$ in cortex and $p = 0.006$ in hippocampus. Neuroprostanes were lower in cortex in the DHA treated group, $p = 0.047$. F₂-dihomo-Isoprostane, an indicator of white matter damage, was significantly lower in tissue from hippocampus in the DHA treated group, $p = 0.035$.

Conclusions Treatment with DHA after severe neonatal hypoxia attenuates lipid peroxidation and brain damage in both grey- and white matter tissues. These novel findings add new knowledge on oxidative injury and points at a possible therapeutic intervention after perinatal asphyxia or severe hypoxia in both term and preterm babies.

Neonatal Brain and Development, Intervention and Outcome

O-057

MELATONIN AS A NOVEL NEUROPROTECTANT IN PRETERM INFANTS – A DOUBLE BLINDED RANDOMISED CONTROLLED TRIAL (MINT STUDY)

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Background Experimental studies suggest that melatonin is neuroprotective. Preterm infants are deprived of the normal intrauterine exposure to maternal melatonin and may benefit from supplementation to adult physiological levels.

Aim To prove that melatonin supplementation to adult concentrations decreases prematurity associated white matter injury assessed by tract based spatial statistics at term equivalent age.

Methods The study was a phase 2 exploratory; multi-centre double-blinded randomised placebo-controlled 2-arm trial, evaluating the neuroprotective effect of melatonin in preterm infants less than 31 weeks gestation. The 2 study drugs, melatonin (active) and normal saline (placebo) were given as an intravenous infusion once a day for 7 days starting by 48 h after birth. The dose of melatonin (0.1 mcg/kg/hr for 2 h) was derived from our previous pharmacokinetic study. Analysis was by intention to treat. Magnetic resonance imaging (MRI) was done at term corrected age. A 5% difference in the fractional anisotropy (FA) on MRI was taken as the primary endpoint.

Results Fifty-eight preterm infants participated in the study; 30 received melatonin and 28 received saline. Four babies died in each group. The 2 groups did not show any differences in the demographic data or in the short term adverse events. Seventeen infants from the melatonin group and 19 from the placebo group had MR images which were analysed. There was no difference in the FA in the 2 groups.

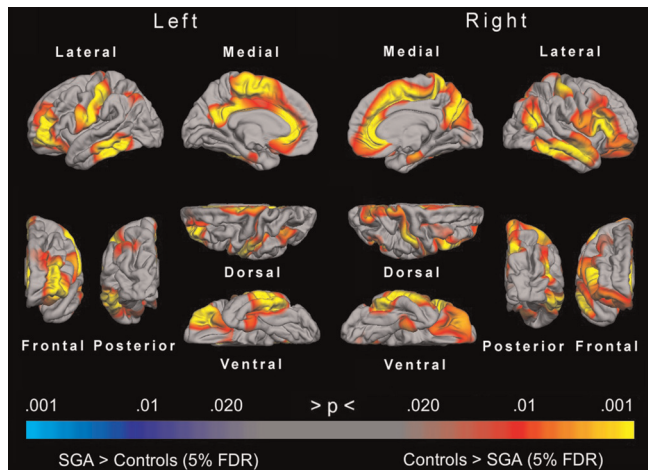
Conclusions Melatonin supplementation to adult physiological levels during the first week after birth did not alter FA in the preterm white matter at term equivalent age.

O-058

BRAIN MORPHOMETRY IN YOUNG ADULTS BORN SMALL-FOR-GESTATIONAL-AGE AT TERM

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Abstract O-058 Figure 1 Group differences in surface area change between SGA young adults and controls. The mapping of cortical surface area reduction in SGA young adults and controls is shown on the reconstructed cortical surface. Cortical areas with statistically significant difference between groups are shown in colour, and the colour scale shows the dynamic range of the statistically significant changes (in p-values), red to yellow represents an increasing expansion of the cortex in SGA group to fit the template, thus surface area reduction in these areas compared with controls. All significant clusters survived FDR correction at $p < 0.05$. No areas with surface area expansion (blue areas) were found in the SGA group compared with controls

Background/aims Being born small-for-gestational-age (SGA), a proxy for fetal growth restriction (FGR) has been related to poor school performance, lower academic achievement and cognitive problems. The aim of this study was to investigate whether young adults born SGA at term had reduced brain volumes, cortical surface area and/or cortical thickness, and whether brain morphometry measures were related to cognitive functioning.

Methods In this population-based follow-up study at age 20, 58 term-born SGA (birthweight < 10 th centile, mean: 2915 g) and 81 non-SGA controls (birthweight > 10 th centile, mean: 3707 g) were included. MRI-examinations at 1.5 T were obtained in 47 SGA and 61 control subjects. Image analysis was performed by the FreeSurfer, version 5.1. IQ was assessed by Wechsler Adult Intelligence Scale 3rd edition (WAIS-III).

Results Total brain volume was smaller in the SGA than in the control group (-5.6%; $p < 0.001$). This reduction included most structures, but relative volumes were the same. Cortical surface area was significantly reduced in the SGA group compared with controls in multiple regions across the cerebral cortex, especially in the frontal, parietal and temporal lobes compared with controls (Figure). The reduction in surface area in the SGA group was most pronounced in the anterior cingulate gyri bilaterally. No associations were found between brain measures and IQ measures in either group.

Conclusions Young adults born SGA at term have a global reduction in brain volume and regional reductions in cortical surface area. This may have long term consequences for cognitive functioning.

O-059 IMPAIRED EXECUTIVE FUNCTIONS IN COMPLEX TASKS IN CHILDREN AND ADOLESCENTS BORN VERY PRETERM

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Introduction Many studies have found impaired performance in executive functions (EF) in children born very preterm (VPT) [1]. EF play a pivotal role for academic achievement and personal autonomy. Demands in both domains and, in parallel, the dependence on EF ability in daily life continuously increase in later childhood and adolescence [2].

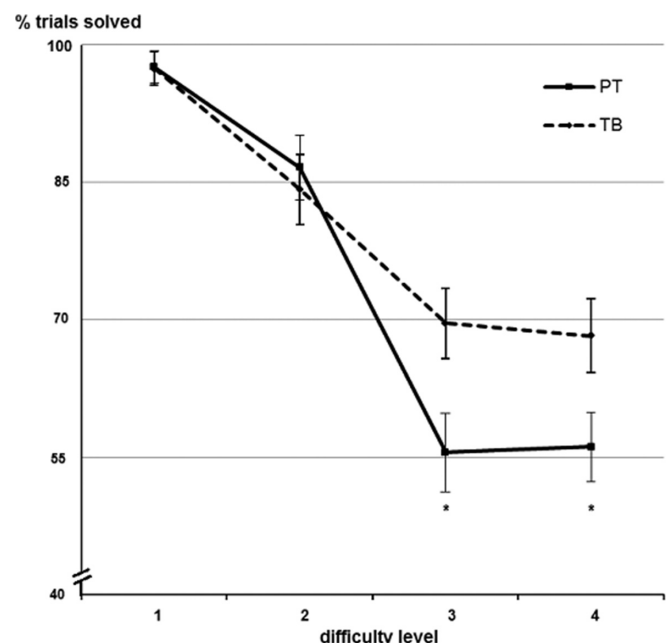
Methods Forty-one VPT children/adolescents between 10 and 16 years with normal general cognitive abilities and 43 healthy term-born (TB) peers were examined. Parents reported on their children's EF ability in the home and school environment using the Behaviour Rating Inventory of Executive Functions, BRIEF. Additionally, computer-based testing using the CANTAB test battery provided objective measures of executive functioning.

Results Parents of VPT children rated EF abilities of their children poorer than parents of TB children, with 10–20% of all VPT children experiencing clinically relevant EF problems vs. none of the TB children. In computerised EF tests, an interaction between birth status and task difficulty was found for various EF components: Performance of VPT and TB children was comparable in lower but poorer in higher difficulty levels for VPT children (e.g., Fig. 1 for planning accuracy).

Conclusions Executive function difficulties in VPT children and adolescents become more pronounced with increasing task demands. As EF demands in daily life become more complex in later childhood and adolescence, EF deficits may hinder optimal development in former VPT children.

REFERENCES

- for a review : Aarnoudse-Moens *et al.*, Pediatrics 2009; Mulder *et al.*, Dev Neuropsychol 2009
- Burnett *et al.*, Early Hum Dev 2013



Abstract O-059 Figure 1 VPT participants solve significantly fewer trials as the level of planning demands increases