

transplants were from living-related donors. At the time of transplantation the mean height z score was -1.15 ± 1.7 and BMI z score was 0.44 ± 1.8 . Eighteen months after transplantation, catch-up growth was seen in 40% of children, 30% had normal linear growth without any catch-up and 30% had slow growth rate after transplantation. Children with evidence of catch-up growth (growth velocity z score >0) had more growth retardation at the time of transplantation, and were receiving lower doses of prednisone at 1.5 years after transplantation. Younger infants (below 6 months) were most likely to demonstrate catch-up growth after transplantation. In summary, a large proportion of children have growth retardation at the time of liver transplantation. Serum albumin increased significantly after (39.8 ± 5.2 g/L) vs before (34 ± 11 g/L) transplantation, and Alanine transferase (ALT) decreased significantly from (130 ± 260 U/L) to (30 ± 15 U/L). Poor growth after transplantation occurred more in those receiving higher doses of corticosteroid. This growth retardation is inversely correlated with age. Growth after transplantation is proportional to the degree of growth retardation at transplantation and inversely correlated to age at transplantation.

165 THE METABOLOMIC PROFILE OF UMBILICAL CORD BLOOD IN NEONATAL HYPOXIC ISCHAEMIC ENCEPHALOPATHY

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Background Hypoxic ischaemic encephalopathy (HIE) is associated with the activation of multiple biochemical pathways. The importance of these pathways individually, and that of their interaction, in the disease process is not fully understood. The aim of this study was to describe and quantify the metabolomic profile of umbilical cord blood samples in a carefully defined population of full-term infants with HIE.

Methods Full-term infants with perinatal asphyxia (with and without HIE) and healthy controls had umbilical cord blood drawn and bio-banked at -80°C , within 3 hours of birth. A combined direct injection and LC-MS/MS assay (AbsolutIDQ p180 kit, Biocrates Life Sciences AG, Innsbruck, Austria) was used for the metabolomic analyses of the samples. The degree of encephalopathy among those with asphyxia was defined using both continuous multichannel-EEG in the first 24 hours, and modified Sarnat score.

Results 142 neonates were included in the analysis (HIE=31, asphyxia without encephalopathy=40, controls=71). There was a significant alteration ($p < 0.01$) in 29 metabolites from 3 distinct metabolite classes (Amino Acids, Carnitines, and Phosphatidylcholines) between study groups. 13 of these metabolites were significantly altered between HIE and controls. Cross-validated Partial Least Square Discriminant Analysis models were developed to distinguish between the groups. The HIE model differentiated significantly between HIE, and those without HIE (AUC=0.93, $R^2 = 0.36$, $Q^2 = 0.25$).

Conclusion The description of the metabolomic profile from umbilical cord plasma and the specific metabolite signature associated with HIE, offers insight into the disease mechanism and the possibility of an early screening test.

166 SIMULTANEOUS ³¹P-MAGNETIC RESONANCE AND NEAR-INFRARED SPECTROSCOPIC INVESTIGATION OF BRAIN TISSUE OXYGENATION, CYTOCHROME-C-OXIDASE AND INTRACELLULAR METABOLITES DURING PERINATAL CEREBRAL HYPOXIA-ISCHAEMIA

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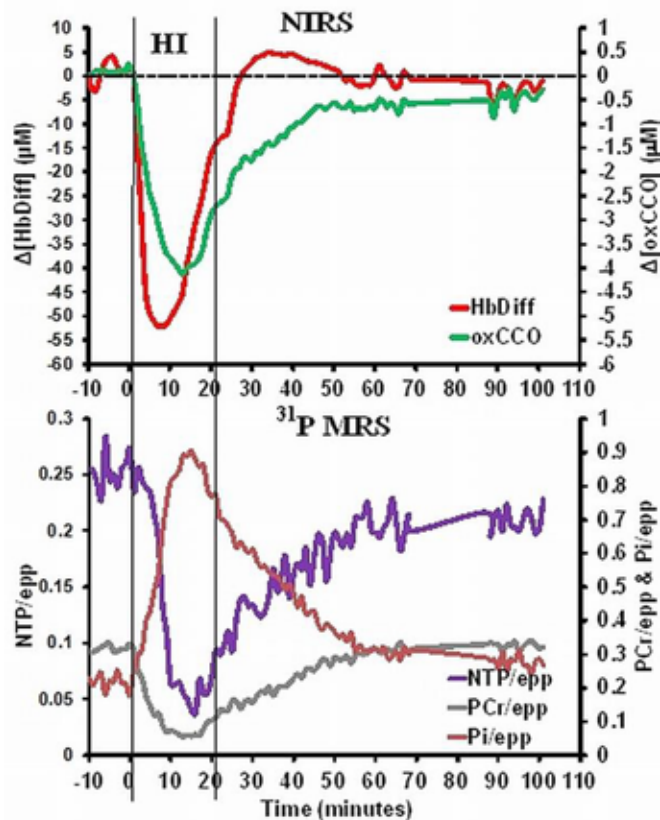
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Background Hypoxic-ischaemic neonatal encephalopathy is associated with high mortality and morbidity rates worldwide.

Aims To investigate brain haemodynamic, cytochrome-c-oxidase (CCO) and energy-resource changes during transient hypoxia-ischaemia (HI) and recovery using simultaneous broadband near-infrared spectroscopy (NIRS) and phosphorus (³¹P) magnetic resonance spectroscopy (MRS).

Methods Nine healthy piglets (aged < 24 hr) were anaesthetised and physiologically monitored. Transient cerebral HI (duration 20 minutes) was induced by reducing the inspired oxygenation and reversibly inflating bilateral carotid artery occluders. Using ³¹P MRS we measured inorganic phosphate (Pi)/epp, phosphocreatine (PCr)/epp, and nucleotide triphosphate (NTP)/epp where epp=exchangeable phosphate pool= $\text{Pi} + \text{PCr} + 3\text{NTP}$. NIRS measured cerebral concentration changes of oxy-haemoglobin (HbO₂) and deoxy-haemoglobin (HHb), and cytochrome-c-oxidase oxidation state changes ($\Delta[\text{oxCCO}]$).

Results Simultaneous ³¹P-MRS and NIRS results are shown. HI rapidly reduced brain oxygenation as shown by changes in haemoglobin difference ($\Delta[\text{HbDiff}] = \Delta[\text{HbO}_2] - \Delta[\text{HHb}]$) closely followed by a fall in $\Delta[\text{oxCCO}]$. PCr/epp fell, and Pi/epp rose, quickly while NTP/epp was buffered initially and only declined when $\Delta[\text{oxCCO}]$ was significantly lowered.



Abstract 166 Figure 1

Discussion During transient HI, CCO becomes reduced due to oxygen depletion; adenosine triphosphate levels are initially preserved by the creatine kinase reaction leading to PCr decline whereas energy utilisation without oxidative phosphorylation leads to increased Pi. Complementary MRS and NIRS enable better understanding of the cerebral metabolic response to HI and can help evaluate early interventional therapies.

167 **MSC-CONCENTRATED SUPERNATANT: A NOVEL THERAPEUTICAL APPROACH IN INFLAMMATION-INDUCED PRETERM BRAIN INJURY?**

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Background and aims Preterm brain injury of premature born infants is a main cause of disability and represents an enormous individual, familial and social burden. Up to 50% of these children suffer from disabilities such as cerebral palsy and cognitive disorders. The aetiology of brain injury has been considered to be multifactorial. Factors such as hyperoxia or inflammation are important pathomechanism in the development of brain injury.

As infections and subsequent inflammation are almost unavoidable on NICUs, new anti-inflammatory approaches are needed. In different experimental settings, mesenchymal stem cells (MSCs) show these anti-inflammatory abilities. Although intravenously administered MSCs get trapped in the lung, therapeutic effects in target tissue are detectable, thereby indicating paracrine mechanisms. Since MSC-supernatants contain molecules with immunosuppressive functions, such as the identified TSG-6, we wondered whether MSC supernatants contain additional, maybe synergistically acting factors. The objective of this study is to evaluate the effect of concentrated MSC-supernatant on brain damage caused by inflammation.

Methods Wistar rats were randomized in 4 groups (vehicle/vehicle, vehicle/concentrated MSC-supernatant, LPS/vehicle, LPS/concentrated supernatant). LPS (0.25mg/kg) was administered at p3, concentrated MSC-supernatant at p3 and p4. At p5, animals were transcardially perfused, brains were removed and snap-frozen for molecularbiological analysis.

Results At p5, LPS-treated animals show a marked increase in apoptosis, whereas additional treatment with concentrated MSC-supernatant results in a decrease in neural apoptosis.

Conclusions Concentrated MSC-supernatant showed promising effects on inflammation-induced brain damage in an experimental model of encephalopathy of prematurity.

168 **SERUM VEG F LEVELS IN PRETERM INFANTS: EFFECTS OF GESTATION AND LASER OR BEVACIZUMAB THERAPY FOR RETINOPATHY OF PREMATURITY**

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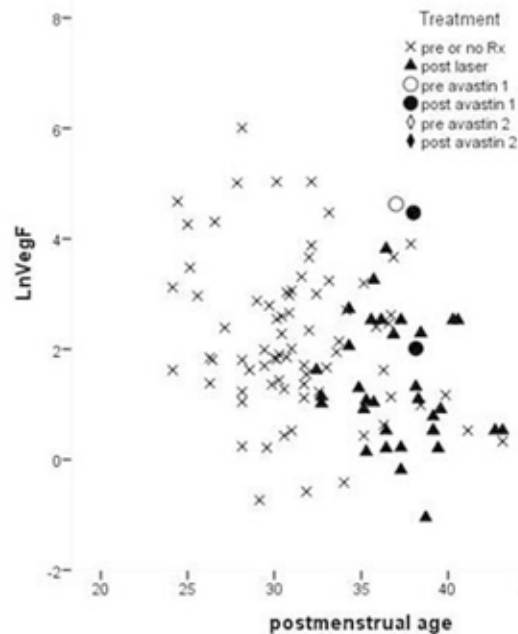
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Background Bevacizumab, a monoclonal antibody to the vascular endothelial growth factor Veg F appears to offer successful treatment of severe retinopathy of prematurity (ROP), but there are no human data addressing potential systemic absorption and effects on systemic Veg F levels in preterm infants. We measured Veg F in preterm infants during their stay in intensive care including some infants treated with laser or bevacizumab for ROP.

Methods Serum and plasma were salvaged as part of a consented research study in preterm infants from delivery to discharge. Veg F levels were measured using flow cytometry and analysed in relation to gestation, postmenstrual age and any ROP treatment.

Results 26 infants, median 26 wks gestational age (range 23–29 wks) contributed 114 samples. 5 received laser treatment for ROP, 2 bevacizumab. Serum VegF levels decreased with increasing

postmenstrual age. Levels for those treated for ROP did not differ from those untreated. The two infants that received bevacizumab had lower VegF levels after treatment than before.



Abstract 168 Figure 1

Conclusions This first data in human preterm infants with and without ROP treatment show trends with increasing postmenstrual age, and that VegF levels in infants treated with bevacizumab do not appear to differ from those untreated or those treated with laser. Individual infants receiving bevacizumab had lower VegF levels in the first week after injection than before. As bevacizumab treatment increases efforts should be made to further assess effects on circulating VegF.

169 **HOSPITAL MORTALITY IN 2,437 INFANTS IN THE AUSTRALIAN, NEW ZEALAND AND UK BOOST II TRIALS OF NEONATAL OXYGEN SATURATION TARGETING**

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Background The optimal oxygen saturation (SpO₂) for preterm infants is unknown. Three BOOST II trials in Australia, New Zealand and UK are comparing outcomes in infants < 28 weeks after randomisation to SpO₂ targeting of 85–89% vs 91–95%, using masked oximeters.¹ In interim analysis the high target increased 36 week survival in infants whose oximeter had been upgraded with new, more accurate software.^{2,3}

Methods Pooled analysis of hospital mortality by target, overall and by old or new software.