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Background Supraphysiologic oxygen concentrations are toxic to the developing brain. Inflammatory processes increase the risk of brain injury. We have previously shown a protective effect of dextromethorphan, a NMDA receptor antagonist and sigma-1 receptor (σ1R) agonist, in an animal model of hyperoxia-induced neonatal brain injury. In adult brain injury, sigma agonists have a proven therapeutic potential.
Aim To assess the highly selective σ1R agonist PRE-084 in a newborn animal model of inflammation-sensitized hyperoxia-induced brain injury.
Methods Rat pups were randomly pre-sensitized with a single intraperitoneal (ip) injection of i) LPS or ii) vehicle on postnatal day 3. On postnatal day 5, pups were ip-injected with i) PRE-084 1μg/g bodyweight or ii) vehicle and were subsequently subjected to either i) hyperoxia (HX, FiO2>0.9) or ii) normoxia (NX, FiO2=0.21) for 24 hours. At the end of exposure, animals were sacrificed and brains were processed for caspase-3 analysis using immunohistochemistry and Western Blotting.
Results A single LPS injection significantly increased the number of activated caspase-3-positive cells in cortical grey matter after hyperoxic exposure, which was reduced by PRE-084 administration (mean number of cells ±SEM; LPS_NX_vehicle 31.26±1.29 vs. LPS_HX_vehicle 38.11±1.13, p<0.01 vs. LPS_HX_PRE-084 33.66±1.54, p<0.05; n=6–7). Western Blot analyses showed a strong reduction in caspase-3 cleavage in PRE-084-treated pups compared to vehicle-injected controls in both pre-sensitized and non-pre-sensitized animals after hyperoxic exposure.
Conclusion PRE-084 reduces inflammation-sensitized hyperoxia-induced injury in the developing rat brain by inhibition of apoptosis. Sigma agonists are a potential therapeutic approach in perinatal brain injury and merit further studies.

1084 ENDOTHELIAL DYSFUNCTION AND PERINATAL MORTALITY OF PRETERM INFANTS EXPOSURED INTRAUTERINE HYPOXIA

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Aim To investigate the endothelial dysfunction in preterm newborns with birth weigth over 1500 gr which died in early neonatal period.
Methods For this purpose 30 surviving and 15 dead newborns with birth weight over1500gr were examined and divided in two groups: control group included 30 newborns, main group-15 infants died in early neonatal period. İn all infants were determined antenatal hypoxia by ultrasonography examination. In order to determine endothelial dysfunction sİCAM-1 and sVCAM-1 concentrations were detected by Uscn (Life Science Inc., USA) kits in 1st-3rd and 5th-7 th days. The Student*t*-test and the Mann-Whitney test were used for comparison of parametric and non-parametric parameters.
Results On the 1st–3rd day the levels of the both adhesion molecules were higher in main group than the control group, but on the 5th–7th days of life they were significantly decreased in comparison with either control group and 1st–3rd days parameters. Adhesion molecules concentations in control group were increased in dynamic (p<0.01).
Conclusion The appointment of the level of adhesion molecules may give an opportunity to determine the endothelial dysfunction and may be predict about perinatal outcome.

1085 CARDIOVASCULAR DYSFUNCTION IN INFANTS WITH NEONATAL ENCEPHALOPATHY IN THE 1ST WEEK OF LIFE

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Background and Aims Perinatal asphyxia may result in transient myocardial ischameia, confirmed by elevated Troponin T levels. Gold standard echocardiographic measures of contractility (ejection and shortening fraction) may not pick up subtle ischaemic changes. Tissue Doppler imaging (TDI) allows assessment of systolic and diastolic function. Used in conjunction with Troponin T TDI may offer superior measure of myocardial contractility.
Methods Term infants with evidence of Neonatal Encephalopathy (NE) underwent echocardiography on Day 1 & 7 of life. Healthy term controls had one echocardiogram on Day 1. Serum Troponin T levels were recorded in infants with NE. Myocardial velocities were obtained using a pulsed wave doppler from an apical four chamber view. Peak systolic (S'), early diastolic (E') and late diastolic (A') velocities were recorded.
Results 17 patients with evidence of NE and 20 term controls were recruited. Mean birthweight (SD) was 3.6 kg (0.9) and gestation 39 (5) weeks. TDI systolic and diastolic velocities increased between Day 1&7 in infants with NE. All day 1 measures in the NE group were less than the controls. There was no significant difference between the shortening/ejection fraction on day 1 between the two groups (NE: 33.7–35.3%; Control: 64.3–67.4%) Troponin levels were significantly elevated on Day 1 compared to Day 7 in NE group (p<0.05) (0.53–0.38ng/ml).
Conclusions TDI measures in infants with NE are less than controls on Day 1. Troponin levels were initially significantly increased providing further evidence of myocardial ischaemia in infants with NE.

1086 SEIZURES ARE ASSOCIATED WITH ALTERED HIPPOCAMPAL DIFFUSION IN NEONATES WITH HYPOXIC-ISCHEMIC ENCEPHALOPATHY

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In animal models, neonatal seizures (NS) alter hippocampal development and lead to long-term deficits. Whether NS similarly affect humans is not known. The goal of this study was to assess whether NS are associated with altered hippocampal microstructure in neonates with hypoxic ischemic encephalopathy.

We included 6 neonates with and 27 without seizures. All were treated with therapeutic hypothermia after birth. Neonatal (median 5 days) and 6-month diffusion tensor imaging was used to measure apparent diffusion coefficient (ADC) from regions of interest (ROIs) in the hippocampus, basal ganglia, thalamus and frontal white matter.

ADC was significantly lower on the 6-month scan as compared to the neonatal scan for all ROIs. There were no significant differences in ADC on the early scan when comparing neonates with and without seizures. At 6 months, infants with seizures as neonates had a 6% higher hippocampal ADC (95% confidence interval: 0–11%, p<0.05). There was no significant difference in ADC for the other ROIs.

These preliminary results suggest that NS are associated with altered hippocampal structural development. Because the difference was seen only in the hippocampus, and on follow-up imaging but

not the neonatal scan, we speculate that NS may have a negative effect on hippocampal development. However, these results could also be explained by unmeasured neoantal hypoxic-ischemic injury. The findings are in keeping with studies that suggest NS are an independent risk factor for adverse neurodevelopmental outcome. Further studies are needed to confirm whether seizures harm newborns.

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1087 INVESTIGATE OF S100B PROTEIN IN SERUM AS PROGNOSTIC MARKER FOR BRAIN INJURY IN TERM NEWBORN INFANTS WITH HYPOXIC ISCHEMIC ENCEPHALOPATHY

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Background Further to investigate whether increased S100 levels in serum are correlated with the grade of HIE after perinatal asphyxia, mechanical ventilation in some severe cases of the asphyxiated infants and more specifically whether increased S100 predicts the cerebral injury and subsequent cerebral palsy.

Methods All risk neonates with severe asphyxia, within 24h of injury were included. Serum S100 was measured on postnatal days 1–3–7 in 62 term infants with birth asphyxia. S100B levels were measured using ECLIA method.

Results The avarage serum S100B levels for the control group(N=48) was 0.12 microgL(–1) (cut-off point). S100B levels were significantly higher in asphyxiated term neonates N=29; M= 0.64. Infants with moderate and severe HIE had significantly higher S100 levels on postnatal day 1 ($p = 0.031$) and day 2 ($p = 0.008$) than infants with mild or no HIE. The levels of S100 decreased on days 2 and 3 in all infants with HIE. The median S100 level on postnatal day 1 was higher in nine infants who died neonatally and in 10 infants who developed cerebral palsy (CP), compared with 43 infants with no signs of impairment at follow up, 14.0 μg/L, 20.7μg/L and 5.5μg/L, respectively. A level of S100 above 12 μg/L the first day of life was significantly more frequent in infants who died or developed CP than in infants with no impairment at follow up ($p = 0.02$).

Conclusion Early determination of serum S100 may reflect the extent of brain damage in infants with HIE after asphyxia.

1088 VENTILATION MODALITY AND CEREBRAL DAMAGE IN PRETERM INFANTS

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Background and Aims Several studies on high frequency oscillatory ventilation (HFOV) have demonstrated a high relation between this method and the incidence of hemorrhagic or ischemic brain injures. In this study, we meant to verify the incidence of intraperiventricular hemorrhage (III–IV stadium) and cystic periventricular leukomalacia (CPVL) in subjects submitted to different ventilation (HFOV vs CMV).

Materials and Methods We have examined 120 newborns (mean gestational age 30±1.85 weeks, mean birth weight 1314±404.14 grams). Group A: 60 infants ventilated in HFOV; Group B: 60 infants ventilated in CMV. All received surfactant.

All infants underwent monitoring of cardiovascular function with evaluation of parameters such as fractional shortening, ejection fraction, size of rooms, the ductal shunt, pulmonary artery pressure and cardiac output and blood pressure.

Results Infants ventilated in HFOV have required a maximum value of MAP significantly lower (p<0.05) versus those ventilated in CMV; Iin group A, 8 (13.3%) experienced a hemorrhage of III–IV degree against 12 (20%) of subjects in group B.

They presented CPVL 14 (7.23%) infants in group A compared with 16 (26.6%) in group B. There were no differences in cerebral blood flow and resistance index of the anterior cerebral artery. There were no differences in cardiac function.

Conclusions Our data show an increase, not statistically significant, of PIVH and CPVL in newborn infants treated with conventional ventilation than oscillatory ventilation. This is attributable to the use of a MAP "optimal" able to obtain a good alveolar recruitment without causing hyperexpansion.

1089 VISUAL EVOKED POTENTIALS IN TERM AND PRETERM INFANTS

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Background and Aims Evoked potentials are a useful non-invasive method for the assessment of neurological status in term and preterm infants at risk for perinatal CNS damage. The present study intended to gather reference values of visual evoked potentials (VEP) for preterm and term neonates and identify neonates at risk for perinatal CNS lesions using VEPs.

Methods 23 healthy preterm and term neonates (group A) and 16 infants with perinatal brain injury (group B) were examined for this study. Groups were classified according to their post-conceptual age (A1/B1: 42–45 weeks, n=4/6; A2/B2: 38–41 weeks, n=5/8; A3: 36–37 weeks, n=12; A4/B3: < 36 weeks, n=2/2). Stimulation was triggered by stroboscopic flashes (1 Hz/10 μs) and P1 and N2 waves were analyzed.

Results Latencies significantly correlated with post-conceptual age (P1: p<0.001, N2: p<0.05) and gestational age (P1: p<0.01). The average latency values (mean±SD) of the subgroups were: group A1 (P1:165.7ms±33.5; N2:211.5ms±29.9), A2 (P1: 199.6ms±34.2; N2:255.6ms±25.8), A3 (P1:223.8ms±14.7; N2:272.1ms±13.5), A4 (P1:240 resp. 209ms; N2:242 resp. 233ms). Average latencies of term infants with or without perinatal injury differed significantly for P1 (228.8 ms±30.9 vs. 165.7ms±33.5; p<0.05) and N2 (266.0 ms±21.1 vs. 211.5ms±29.9; p<0.01).

Conclusions The present study adds to the knowledge on normal VEP values during early development. Present data showed a negative correlation with post-conceptual age for central latencies as an equivalent of progressing myelination regardless of extra- or intrauterine maturation. Term infants with perinatal brain injury showed significantly prolonged VEP latencies compared to healthy children.

1090 RELATIONSHIP BETWEEN NEUROTROPHINS AND BRAIN STRUCTURE IN PRETERM GROWTH RESTRICTED BABIES

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Background Neurotrophins are responsible for the growth and survival of neurons during early brain development. Intrauterine growth restriction (IUGR) leads to alterations in brain structure.

Aim To explore the relationship between neurotrophins and brain structure in preterm IUGR babies.