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 dexmethylorphan, 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 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.

ENDOTHelial Dysfunction and PERINATAL MORTALITY of PRETERM INFANTS EXPOSED INTRAUTERINE HYPOXIA

doi:10.1136/archdischild-2012-302724.1084

PA Oryuva, HA Saadat, S Safikhani, A Saadat, M Sewing, M Tarana. Azerbaijan Medical University; Neonatology; Azerbaijan Medical University; Maternity Hospital, Baku, Azerbaijan

Aim To investigate the endothelial dysfunction in preterm newborns with birth weight over 1500 gr which died in early neonatal period.

Methods For this purpose 30 surviving and 15 dead newborns with birth weight over 1500gr were examined and divided in two groups: control group included 30 newborns, main group-15 infants died in early neonatal period. In all infants were determined antenatal hypoxia by ultrasonography examination. In order to determine endothelial dysfunction sICAM-1 and sVCAM-1 concentrations were detected by Uscn (Life Science Inc., USA) kits in 1st-3rd and 5th-7th days. The Student-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 concentrations 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.

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

doi:10.1136/archdischild-2012-302724.1086


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 ischaemic 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 neonatal 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.

Acknowledgements NIH/NCRR (UL1 RR024131); NIH/NINDS P50NS035902.

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

doi:10.1136/archdischild-2012-302724.1087

1AN Sofjanova, K Piperkova, OV Jordanova. Neonatal and Pediatric Intensive Care; 2Department of Neonatology, University Children’s Hospital, Skopje, FYR Macedonia

**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 average serum S100B levels for the control group(N=48) was 0.12 mcg/L (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 (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**

doi:10.1136/archdischild-2012-302724.1088

A Arco, GT Pagano, G Gitto, S Aversa, I Barberi. Pediatric, University of Messina, Messina, Italy

**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 injuries. In this study, we meant to verify the incidence of intraventricular hemorrhage (III–IV stadium) and cystic periventricular leukomalacia (CPVL) in subjects submitted to different ventilation (HPOV vs CMV).

**Materials and Methods** We have examined 120 newborns (mean gestational age 36±1.85 weeks, mean birth weight 1514±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 ducal 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, in 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 PVH 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**

doi:10.1136/archdischild-2012-302724.1089

F Brackmann, S Scheu, R Trollmann. Department of Pediatrics, University of Erlangen-Nürnberg, Erlangen, Germany

**Background and Aims** Evoked potentials are a useful noninvasive 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/B4: < 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: r<0.001, N2: r<0.05) and gestational age (P1: r<0.01). The average latency values (mean±SD) of the subgroups were: group A1 (P1:165.7±33.5, N2:211.5±29.9), A2 (P1: 199.6±34.2; N2: 255.6±25.8), A3 (P1:223.8±14.7; N2:272.1±13.5), A4 (P1:240 resp. 209ms; N2:242 resp. 235ms). Average latencies of term infants with or without perinatal injury differed significantly for P1 (228.3±30.9 vs. 165.7±33.5; p<0.05) and N2 (266.0±21.1 vs 211.5±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**

doi:10.1136/archdischild-2012-302724.1090

1 JL Parke, 2 J Atkinson, 3 J Miyan, 4 A Hendrickson, 5 S Victor. 1L Parkes, 2J Atkinson, 3J Miyan, 4A Hendrickson, 4,5S Victor. 1Neonatal and Pediatric Intensive Care; 2School of Health Sciences, University of Manchester, Manchester; 3School of Health Sciences, University of Liverpool, Liverpool; 4Faculty of Life Sciences, University of Manchester; 5Newborn Intensive Care Unit, Central Manchester University Hospitals NHS Foundation Trust; 6School of Biomedicine, University of Manchester, Manchester, UK

**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.