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EFFECT OF REPEATED ASPHYXIA/REVENTILATION ON STRIATAL DOPAMINE RELEASE AND CEREBRAL CORTICAL OXYGEN PRESSURE IN NEWBORN PIGLETS. Jan M. Goplerud, Chao-Ching Huang, Masahiko Yonetani, Maria Delivoria-Papadopoulos and Anna Pastuszko. Dept.s of Physiology, Biochem/Biophysics and Pediatrics, University of Pennsylvania School of Medicine, Philadelphia, PA, U.S.A.

The striatum, richly innervated by the nigrostriatal dopaminergic pathway, is a brain region highly vulnerable to ischemic/hypoxic neuronal damage and especially affected by repetitive insults. The present study tests the hypothesis that recurrent asphyxia/reventilation alters extracellular dopamine (DA) by decreasing cerebral cortical oxygenation in the striatum of newborn piglets. Anesthetized, ventilated piglets (n=7) underwent seven repeated episodes of 3 min asphyxia, each followed by 15 min reventilation/recovery. Cortical O_2 pressure, by phosphorescence quenching, and extracellular striatal DA, by in vivo microdialysis, were measured continuously. Serum lactate levels increased from 4±3 mM (baseline) to 16±1 mM/L after the 7th episode of asphyxia/ reventilation. Cortical O_2 pressure decreased from 39±9 Torr (baseline) to 11±6 Torr during each asphyxia then rapidly returned to baseline values, except after the 7th asphyxia when it returned to baseline in 10 min then decreased again to 19±4 Torr. Extracellular DA concentration was dependent on the number of asphyxia episodes and was higher after each successive asphyxia. From the 2nd to 7th asphyxia, extracellular DA increased from baseline of 6.5 to 9, 12.6, 26, 57, and 84 pmoles/ml, respectively. During 15 min reventilation, DA returned to baseline levels for the first 5 asphyxias, but after the 6th and 7th episodes, DA remained higher than baseline by 50-70%. This progressive DA accumulation could result from hypoxia-induced DA release or from impaired DA reuptake and/or degradation. Thus, repeated episodes of asphyxia were associated with progressive disturbance of striatal DA metabolism, leading to high levels of extracellular DA which represent a potential mechanism of post-asphyxial striatal neuronal injury. Funded by NIH #HD-20337.

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Inhibition of surfactant in-vitro properties by various proteins

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Background: Both surfactant (SF) deficiency, anomalies in synthesis and inactivation are major pathophysiological features of neonatal RDS. We previously could show, that tracheal aspirates from preterm infants with RDS containing increased amounts of proteins exhibit abnormal surface properties in the pulsating bubble model (1). **Aim:** We therefore aimed to quantify inhibition of surface properties by various proteins in-vitro using the pulsating bubble surfactometer (PBS). **Methods**: Bovine surfactant (Alveofact®) was diluted with 0.9% saline to a 1 mg/ml phospholipid-concentration and further incubated with various concentrations of albumin, fresh plasma, α_2-macroglobulin and α_1-antitrypsin (n = 4 at each concentration). The surfactant-protein samples were examined in the PBS, surface properties were evaluated after 150 pulsating cycles. **Results:** Data for γ max. (maximum surface tension; mN/m) are given as mean/SD in table 1.

	Controls	0.05	0.1	1	5
Albumin[mg/ml]	40.00 ± 3.56		45.5 ± 2.38	54.50 ± 3.87	56.50 ± 2.16
Fresh plasma [mg/ml]	42.75 ± 0.96	38.4 ± 2.30	---	46.25 ± 5.51	53.00 ± 4.08
α_2-macroglobulin [mg/ml]	40.00 ± 4.32	60.3 ± 1.71	64.0 ± 1.15	64.50 ± 3.11	---
α_1-antitrypsin [mg/ml]	40.00 ± 3.12	---	41.5 ± 2.47	47.50 ± 4.12	46.25 ± 3.12

Conclusions: Inhibition of SF-function was most obvious following incubation with α_2-macroglobulin, which is of particular importance for mechanisms of inactivation and further development of SF-preparations resistant to inactivation.

1) Gortner, L. et al. Pediatr Res 32: 635 A (1992)

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***IN VIVO* PROTON MAGNETIC RESONANCE SPECTROSCOPY (^{1}H-MRS) IN CYSTIC LEUCOMALACIA OF INFANCY.** Floris Groenendaal, Paula Eken, Jeroen van der Grond, Karin Rademaker, Linda S. de Vries. Departments of Neonatology and Radiology, Wilhelmina Children's Hosp/ Utrecht Univ Hosp, Utrecht, the Netherlands

To test the hypothesis that cerebral metabolic disturbances could be demonstrated *in vivo* in neonates with subcortical (SCL) and periventricular cystic leucomalacia (PVL) 7 infants (gestational age 29.1 to 40.4 weeks, 4 preterm--PT, 3 fullterm--FT, birth weight 1050 to 4050 g) with cystic leucomalacia (CL), as diagnosed by cerebral ultrasonography, were examined using ^{1}H-MRS. Methods: ^{1}H-MRS was performed at a postmenstrual age of 42.1±2.5 wks (40-47 wks), 5.8±4.7 wks (2 days - 12 wks) after cerebral ischemia. In a 1.5 T magnetic field, MR spectra were obtained in a 225 mm field of view, a volume of interest (VOI) of 7x5x2 cm. Pulse sequences included adiabatic pulses for water suppression, followed by 90°-180°-180° pulses. One FT neonate died, the 6 survivors were seen for neurodevelopmental follow-up at 3, 6 and 9 months. Results: In the 3 FT with SCL N-acetyl-aspartate/choline (NAA/Cho) ratios of the VOI were 0.49, 0.69, and 0.74 respectively (normal FT neonates >0.85), whereas in the 4 PVL-infants these ratios were 1.01±0.17 (range 0.86-1.24). Lactate resonances at 1.33 ppm, which cannot be demonstrated in normal FT, were found in 2 neonates with SCL (lactate/NAA ratio: 1.07, and 1.59). Lactate was present up to 12 wks after cerebral ischemia in one PVL-infant (lactate/NAA: 0.29). Three others had resonances at 1.3 ppm that could not be discriminated from fat. All 3 SCL-neonates had a poor outcome: one died, 2 showed spastic quadriplegia and cerebral visual impairment. Of the 4 PVL-infants, one appeared to be normal at 9 months of age, two had a suspect neuromotor development on follow-up, and the fourth developed spastic diplegia. Conclusion: using ^{1}H-MRS, cerebral metabolic abnormalities were demonstrated *in vivo* in infants with CL. Lowest NAA/Cho ratios, reflecting severe loss of neurones, were found in the infants with SCL, who had a very poor outcome.

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CEREBRAL NITRIC OXIDE SYNTHETASE ACTIVITY FOLLOWING HYPOXIA IN NEWBORN PIGLETS. Floris Groenendaal, Om P Mishra, David J Hoffman, and Maria Delivoria-Papadopoulos. Departments of Physiology & Pediatrics, University of Pennsylvania School of Medicine, Philadelphia, USA.

Recent studies in animal models suggest, that nitric oxide (NO), produced by nitric oxide synthetase (NOS) during conversion of L-arginine into L-citrulline, is a source of free radicals following hypoxia. The present study tested the hypothesis that NOS was altered in cortical tissue after one hour of cerebral hypoxia. Newborn piglets (6 hypoxia, 6 normoxia) were anesthetized and ventilated; hypoxia was induced by lowering the FiO_2 to 0.05-0.07 in the hypoxia group, and was maintained for one hour. Cerebral cortical tissue obtained from each piglet was homogenized and dialyzed for 6 hours to remove endogenous arginine. The activity of NOS was assessed using the conversion of ^{3}H-L-arginine into ^{3}H-L-citrulline in the presence of calcium and NADPH, followed by counting the amount of ^{3}H-L-citrulline formed after removal of ^{3}H-L-arginine by ion-exchange. Due to NOS activity NO and ^{3}H-L-citrulline are formed on an equimolar basis. Results showed, that NOS activity was present in both groups: normoxia: 265±85, hypoxia: 230±165 fmol NO/mg protein/min. Differences between the hypoxia and normoxia groups were not significant. The results indicate that cerebral NOS in newborn piglets is resistant to hypoxia. The present *in vitro* data do not preclude, that NOS activity is increased *in vivo* during hypoxia by a cellular influx of calcium, thereby possibly contributing to the formation of free radicals and membrane lipid peroxidation following hypoxia. *Funded by NIH #HD-20337, USA and Ter Meulen Fund, the Netherlands.*

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***IN VIVO* EFFECT OF 3-(2-CARBOXYPIPERAZIN-4-YL)PROPYL-1-PHOSPHONIC ACID (CPP), AN ANTAGONIST OF THE NMDA RECEPTOR, ON PORCINE BRAIN CELL MEMBRANE Na^+,K^+-ATPase.** Floris Groenendaal, Karen I. Fritz, Jane E. McGowan, Om P. Mishra, Anli Zhu, Maria Delivoria-Papadopoulos. Depts Physiology & Pediatr, Univ Pennsylvania, Philadelphia, USA.

Hypoxia has been reported to decrease Na^+,K^+-ATPase activity and modify the NMDA receptor in cell membranes of the cerebral cortex of newborn piglets. CPP, a glutamate antagonist of the NMDA receptor, has been shown to reduce cerebral injury in animal stroke models. The present study tested the hypothesis that *in vivo* administration of CPP could preserve brain cell membrane Na^+,K^+-ATPase acitvity during hypoxia. Studies were performed in 18 anesthetized, ventilated newborn piglets (9 normoxic controls--Nx, 4 CPP-treated normoxic--CPP-Nx and 5 CPP-treated hypoxic--CPP-Hx animals). Hypoxia was induced by lowering the FiO_2 to 0.05-0.07 in the CPP-Hx group, and was maintained for one hour. CPP-Hx animals received CPP 30 min prior to the decrease in FiO_2. Both CPP-Nx and CPP-Hx groups received CPP 2 mg/kg IV. Brain cell membrane Na^+,K^+-ATPase activity (μmol Pi/mg protein/hr) was decreased in CPP-Hx (37.0±3.6) and CPP-Nx (35.0±1.6) groups compared to the Nx (46.9±4.6) group ($P<0.05$), indicating that 2 mg/kg CPP did not prevent the decrease of brain cell membrane Na^+,K^+-ATPase activity following hypoxia. These results could be due to either a too low dose of CPP, or an overwhelming release of free radicals during one hour of severe hypoxia. Alternatively, given that *in vitro* CPP does not alter the enzyme activity, the unexpected decrease of Na^+,K^+-ATPase activity in the CPP-Nx group might be due to metabolites of CPP. *Funded by NIH #HD-20337,USA and Ter Meulen Fund, the Netherlands.*

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THE ONSET OF WALKING INDEPENDENTLY: ARE THERE QUALITATIVE DIFFERENCES BETWEEN PRETERM AND FULLTERM INFANTS?

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There are marked individual differences in the ages at which children acquire the ability to walk without support. It is also known that children who are late in acquiring this ability have a higher risk for developmental disorders. Less attention has been paid to the quality of movement expressed in the first attempts at walking alone. Qualitative assessments of early walking may provide a sensitive means for detecting those infants with developmental impairments.

The aim of the study was to devise a standardised instrument for the qualitative assessment of early walking in the free field situation. To control for differences in walking experience, all subjects were assessed 14 days after being able to walk 5 metres independently.

The study group consisted of 52 children of whom 33 were born prematurely (PT) (and further distinguished in terms of being small (SGA)- or appropriate (AGA)-for-gestational age) and 19 were fullterm infants (FT). Walking performance was judged to be optimal, near poor and poor based on a number of criteria.

The optimal criteria were met by 12 PTAGA infants and 1 PTSGA. There were 2 FT, 1 PTAGA and 5 PTSGA in the near poor group. 8 PTAGA and 6 PTSGA but no FT children showed poor walking quality. Those who were SGA were overrepresented in the near poor and poor categories.