143

INCREASED CSF-LEVELS OF EXCITOTOXIC AMINO-ACIDS AFTER FULL-TERM PERINATAL ASPHYXIA. Mats Blennow[1], Henrik Hagberg[3], Eva Thornberg[4], Klara Thiringer[4], Ingmar Kjellmer[2] and Hugo Lagercrantz[1]. Depts of Pediatrics, Karolinska Institute[1] and Gothenburg University[2], Histological Institution[3] and Institution of Pediatric Anaestesia[4], Gothenburg University, Sweden.

The excitatory amino-acids (EA, eg. glutamate and aspartate) are believed to be of major importance in the pathogenesis of neuronal damage in hypoxic-ischemic brain injury. Studies in immature animal-models of asphyxia have shown an extracellular accumulation EA. The deleterious effect of EA on the neuron is supported by the fact that the administration of receptor-antagonists is beneficial in experimental models.

Agonist-operated receptors are well developed in the immature human brain and receptor-density is high in those regions most susceptible to hypoxic-ischemic damage. We have examined the levels of excitatory amino-acids in full-term asphyctic neonates.

Spinal taps were performed in neonates with signs of intrapartum asphyxia (n=10 , gestational age 36-42 w, 0-2 days postpartal age) and non-asphyctic neonates without signs of cerebral disease (n=8,GA 29-42 w , 0-13 days postpartum). Amino-acids were analyzed by chromatography (μmol/l).

Results and conclusions: Aspartate (2.72± 1.16 vs 0.66± 0.08) and glutamate (7.92±4.72 vs 1.15± 0.19) differed significantly between asphyctic and non-asphyctic neonates. In the asphyctic group, interindividual differences were high, and further analyzis will show whether high levels correlate with prognosis or not.

144

ACTIVATION OF THE NORADRENERGIC SYSTEM IN THE RAT BRAIN AT BIRTH. Hugo Lagercrantz & Jean-Marc Pequignot. Department of Pediatrics, (KS), Karolinska Institute, Stockholm, Sweden and Physiologie, Faculté de Medecine, Université Claude Bernard, Lyon, France.

The fetus is sensory deprived and some of its behavioural functions are inhibited. This inhibited state is immediately reversed at birth, the newborn infant is awake and aroused. We now wanted to study how the noradrenergic activity in the brain is related to this excitation at birth.

Noradrenalin (NA)-turnover was studied in the cortex and pons-medulla of rat fetuses and pups. The ratio between the NA-metabolite 3-methoxy-4-hydroxy-penylethylene glycol (MHPG) and NA was determined by HPLC and used as an index of NA-turnover.

Results: The MHPG/NA-ratio was 0.094 in the pons-medulla of fetuses and 0.27 ($p < 0.05$) in the one day old pups. The cortex ratio increased from 0.082 to 0.30 ($p < 0.05$). The index of NA turnover increased significantly already one hour after birth when the pups were exposed to air. If the pups were kept in hypoxic environment, the NA-turnover increased less.

We conclude that the NA-turnover is considerably enhanced after birth if the pups are born in normoxic environment but not in hypoxia. This reflects the activation of the noradrenergic nerves in the brain, which to a large extent originate from the locus coeruleus in the brain stem. We believe that in this way the brain is aroused to new stimuli, e.g. the extra-uterine environment.

145

RELATION BETWEEN BETA ENDORPHINS (ßE) AND CLINICAL INDEXES OF STRESS IN SICK PRETERM INFANTS: EFFECT OF FENTANYL (F). Isabelle Hamon,Jean-Michel Hascoët,Eric Thorin,Bernard Kerdelhué,Paul Vert. INSERM U272, Lab Pharm Cardiovasc, Nancy; INRA, Jouy en Josas; FRANCE

The routine evaluation of stress and efficiency of its prevention remain difficult in preterm infants. A study was prospectively done to assess the best clinical indexes of acute stress and the effect of F treatment in 7 preterm infants, 32-35 weeks gestational age. The infants, 24-48 h old, were mechanically ventilated for respiratory distress syndrome (RDS). Assessment of behavioral state, heart rate (HR), blood pressure (BP), transcutaneous PO2 and SaO2 was done throughout the study. The arterio-alveolar O2 ratio (a/AO2) was calculated as an index of RDS severity. Routine endotracheal suctionning was considered as an acute stress. Measurements of ßE plasma levels were done before and after the suction as biological evidences of stress. The same procedure was performed 2 h later, after IV infusion of 3μg/kg of F, the infants being their own control.

Results: 1) There was a significant linear relationship between ßE and the following parameters: HR (r= 0.397 p=0.041), PO2 (r= - 0.413 p=0.032) and a/AO2 (r= - 0.469 p=0.014), but not with behavior, BP nor SaO2.

2) Effect of F on the acute stress [δ = post- minus pre- suction values]:

		δ ßE (pg\ml)	δ HR (bpm)	δ BP (mmHg)	δ PO2 (mmHg)	δ SaO2 (%)	δa/AO2
Without F	[Mean]	**12.6**	**- 6.6**	**1.8**	**-33.0**	**-12.0**	**-0.12**
	[SD±]	12.2	35.0	6.6	11.2	3.9	0.07
With F	[Mean]	**0.6**	**0.4**	**-2.1**	**-17.4**	**- 6.4**	**-0.06**
	[SD±]	10.3	13.7	3.2	18.1	5.1	0.04
(Wilcoxon) :	p	***.032***	.398	.150	***.046***	***.040***	***.046***

Conclusions: 1) The clinical indexes related to ßE were HR,PO2 and a/AO2.
2) F blunted the alterations of PO2, SaO2 and a/AO2 related to stress.

146

THE MECHANISMS FOR APPARENT LIFE-THREATENING EVENTS Martin P Samuels, Christian F Poets, Jane P Noyes, David P Southall. Department of Paediatrics, National Heart and Lung Institute, Royal Brompton Hospital, London.

Infants with a history of an apparent life-threatening event that received mouth-to-mouth resuscitation (ALE-R) are high risk for sudden death (SID). Investigation of 114 infants (median age 2.8 months; 15 with SID in siblings; 20 born preterm) who had single (n=64) or recurrent (50) ALE-R revealed, compared to controls [1,2], 38 with abnormal hypoxaemia on a 12 hour physiological recording (with accompanying clinical events in 21). Home event recording of TcpO2, breathing movements, ECG ± SaO2 was performed in 46 infants for a median duration 1.4 months: this produced further physiological data in 22 infants.

In 49 infants, mechanisms for ALE-R were found, including: respiratory events suggestive of intrapulmonary shunting (n=29), seizure induced hypoxaemia (7), imposed upper airway obstruction (7), fabricated history/data (4) and pallor without hypoxaemia/arrhythmia (3). 104 infants underwent home TcpO2 monitoring (median duration 6 months): 2 patients died suddenly - non-compliance (1) & discontinued pO2 monitor (1).

Multi-channel physiological recordings ± event capture can provide information relevant to the diagnosis and management of these infants.

[1] Stebbens VA, Poets CF, Alexander JR et al. Arch Dis Child 1991;66:569-573
[2] Poets CF, Stebbens VA, Alexander JR et al. Arch Dis Child 1991;66:574-578

147

RELIABILITY AND RESPONSE TIME OF THREE PATIENT TRIGGERED INFANT VENTILATORS. **Graham Bernstein, John P. Cleary, J. Fernando Rosas, Larry D. Schellenberg, Frank L. Mannino and Gregory P. Heldt. Dept. of Pediatrics, University of California, San Diego, CA., USA.**

We compared the reliability and response time (RT) of three patient triggered infant ventilators in 10 healthy adult rabbits. Ventilation was randomly assigned to a Bear Cub Enhancement Module (CEM), Infrasonics Star Sync, and Draeger Babylog 8000 in both the synchronized intermittent mandatory ventilation (SIMV) and assist-control (A/C) modes. All studies were repeated at ventilator flow rates of 6 and 12 lpm, and at 3 sensitivity settings (except Star Sync). Rabbits were lightly anesthetized and tracheostomized; airway flow and pressure, and pleural pressure were recorded. RT was measured from the start of each spontaneous breath to the onset of each triggered ventilator breath (N=250±50 breaths). Ventilator breaths occurring >200 msec after the start of spontaneous breaths or during early expiration were considered trigger failures and were excluded from analysis for RT. RT (mean±SD) and failure rate at maximum sensitivity and 12 lpm were compared by ANOVA:

	SIMV(msec)	Failure Rate	A/C(msec)	Failure Rate
Star Sync	**50±13**	**0.4%**	**53±15**	**0%**
Bear CEM	**62±11**	**2.3%**	**69±17**	**0%**
Babylog	**97±35**	**20±13%**	**94±24**	**0%**

RT of each ventilator was the same at 6 and 12 lpm in both modes. RT of Star Sync was shorter than Bear CEM, and Bear CEM was shorter than Babylog on both modes ($p<.01$). Decreasing trigger sensitivity by 2 settings increased RT of both Bear CEM and Babylog by 60%. The Babylog failed consistently on SIMV but not at all on A/C.

148

DIAPHRAGMATIC EFFORT AND LUNG MECHANICS ON CONVENTIONAL AND SYNCHRONIZED INTERMITTENT MANDATORY VENTILATION (IMV/SIMV). **J. Fernando Rosas, John P. Cleary, Frank L. Mannino, Graham Bernstein, Gregory P. Heldt. Dept. of Pediatrics, Univ. of California,San Diego, CA, U.S.A.**

We compared lung mechanics and EMG amplitude and duration of 11 rabbits during IMV and SIMV (Star Sync®), before and during resistive loading. SIMV response time was 50 ±13 msec. We recorded airway flow, pleural pressure, lung volume (jacket plethysmograph) and EMG (needle electrodes in the diaphragm). We computed compliance (C), resistance (R), inspiratory work (W) and tidal volume (TV) for mechanical breaths.

Baseline	**IMV**	**SIMV**	**p (ANOVA)**
C (ml/cm H_2O)	**1.79 ±0.29**	**1.88 ±0.24**	**.045**
R (cm H_2O/L/sec)	**30.4 ±5.86**	**30.8 ±5.27**	**.788**
W (g.cm H_2O)	**91 ±15.5**	**105 ±20.2**	**.006**
TV (ml/kg)	**6.2 ±0.9**	**6.4 ±0.9**	**.022**
EMG dur.	**100% (baseline)**	**80%**	**.037**
EMG amp.	**100% (baseline)**	**80%**	**.076**
Resistive loading			
C (ml/cm H_2O)	**2.22 ±0.76**	**2.30 ±0.71**	**.421**
R (cm H_2O/L/sec)	**71.3 ±41.3**	**76.5 ±44.9**	**.032**
W (g.cm H_2O)	**121 ±43**	**142 ±35**	**.018**
TV (ml/kg)	**6.1 ±0.9**	**6.3 ±1.0**	**.276**
EMG dur. (% of baseline)	**120%**	**104%**	**.016**
EMG amp. (% of baseline)	**141%**	**121%**	**.006**

End-expiratory lung volume did not vary. Baseline C, W and TV, and loaded R and W were greater on SIMV. EMG dur. and amp. (% of baseline IMV) were significantly less on SIMV than on IMV.This suggests that ventilator efficiency is increased and diaphragmatic effort is spared by SIMV compared to IMV.