23

CEREBRAL BLOOD VOLUME AND CYTOCHROMEOXIDASE A/A3 DURING INDOMETHACIN APPLICATION. *Hubert Fahnenstich, Anja Broekmans, Stephan Schmidt* and Sabina Kowalewski. Departements of Neonatology and Obstetrics*, Friedrich-Wilhelms-University, Bonn, Germany*

A decrease in cerebral blood flow and in cerebral blood flow velocity caused by indomethacin administration is well known (Child Neurol 1987;29:776-82; Eur J Pediatr 1988;147:315-6). For a deeper view on the cellular base we studied seven premature infants (1080g, 30+2 weeks), who received indomethacin for closure of PDA (0.2 mg/kg weight, i.v.) with the near infrared technique. Cerebral blood volume (CBV) decreased in every child exept one just after starting the indomethacin administration and remained on a lower level during the monitoring time (30 min). The balance of the redox state of cytochrome a/a3 shifted to a decrease of the oxidised part of the enzyme. Table 1 shows the relative concentration change of the CBV and the CYT.

Table 1:

	time 1	*3*	*10*	*30*	*[min]*
CBV	*-0,19*	*-0,189*	*-0,156*	*-0,137*	*[mmolx1^{-1}]*
CYT	*-0,022*	*-0,029*	*-0,025*	*-0,011*	*[mmolx1^{-1}]*

Indomethacin reduced CBV and has a negative effect on the redox state of cytochrome a/a3 as seen by NIRS. Both effects could damage brain cells.

24

AMINOPHYLLINE REDUCES CYTOCHROME C OXIDASE IN THE BRAIN OF PREMATURE INFANTS. Bucher Hans-Ulrich, Wolf Martin, Keel Matthias, Duc Gabriel. Department of Pediatrics, University of Zurich, Switzerland.

Background: The influence of Aminophylline on cerebral perfusion and metabolism in premature infants is controversial. Cytochrome c oxidase is an indicator of aerobic energy production in the cell and can be monitored in the neonatal brain by near infrared spectroscopy (Jöbsis, 1977; Wyatt, 1989).

The **aim** of this study was to investigate the change of oxidised cytochrome c oxidase in the brain of premature infants after a bolus injection of 6 mg Aminophylline per kg body weight administered within 1 to 2 minutes to facilitate weaning from the respirator.

Patients: 13 premature infants (gestational age 26 to 34 weeks, postnatal age 1 to 7 days, birth weight 760 to 2300 g).

Results: Values are means (SD). ΔCBV: change of cerebral blood volume, ΔCyt: change of oxidised cytochrome c oxidase, *:p<0.02.

	before		*3 to 10 min*		*11 to 20 min after injection*
Heart rate	147 (20)	*	158 (28)	ns	156 (23)
tcPco2 (kPa)	5.3 (0.9)	*	4.7 (1.0)	ns	4.7 (0.9)
ΔCBV(ml/100g)	0	ns	-0.04(0.08)	ns	-0.05(0.14)
ΔCyt (µmol/l)	0	*	-0.28(0.34)	ns	-0.28(0.43)

Conclusion: Aminophylline reduces cytochrome c oxidase significantly in the brain of premature infants and seems to interact with energy metabolism.

25

TAURINE CONCENTRATIONS IN BRAIN OF PRETERM AND TERM NEWBORNS MEASURED BY IN VIVO ^{1}H-MRS AND CHROMATOGRAPHY IN AUTOPSY TISSUE. P.S.Hüppi, C.Fusch, C.Boesch, R.Burri, S.Posse, F.Lazeyras, E.Bossi, M.Amato and N.Herschkowitz, Department of Pediatrics, University of Berne, Switzerland

Our study presents data on in vivo measurements of regional Tau concentrations in different stages of early human brain development. We used the method of short echotime ^{1}H-spectroscopy in single volumes of 3.3cm^3 for the in vivo assessment. 27 preterm (≥37wk) and 22 term newborns (≥38wk), all fed maternal milk, were examined by ^{1}H-MRS either in cerebellum or cerebrum. In comparison age-corresponding autopsy tissue was examined by high performance liquid chromatography (HPLC).

Tau:	**Cerebellum** (mM) Autopsy (HPLC) / ^{1}H-MRS	**Cerebrum** (praecentral) (mM) Autopsy (HPLC) / ^{1}H-MRS
Preterm	1.85±0.45/1.51±0.69	2.00±0.36/1.51±1.01
Term	2.48±0.41/2.93±1.78	1.93±0.15/1.52±0.82
	p<0.05/p<0.05	n.s./n.s.

Concentrations of Tau measured in vivo by ^{1}H-MRS and in autopsy tissue by HPLC are comparable. In cerebellum Tau concentration increases from preterm to term newborns.

Cerebellar Tau concentrations measured in autopsy tissue of term newborns are significantly higher than cerebral Tau concentrations (p<0.05). The same tendency is observed in the in vivo ^{1}H-MRS data.

26

BETA-ENDORPHIN IMMUNOREACTIVITY (BEI) IN CSF CORRELATED WITH BRAINSTEM GLIOSIS AND WITH HYPOXANTHINE (HX) IN CORPUS VITREUM LIQUOR IN VICTIMS OF SUDDEN INFANT DEATH SYNDROME (SIDS). Hanne Storm, Karl L. Reichelt, Torleiv O. Rognum and Ola D. Saugstad, Departements of Pediatrics and Institute of Forensic Medicine, Rikshospitalet, Oslo, Norway.

Beta-endorphin is released during stress and activates receptors in ncl. tractus solitarius and induces bradycardia and respiratory depression.

We measured BEI in CSF, in caudal area of ncl. tractus solitarius, brainstem gliosis by immunohistochemistry and HX in corpus vitreum liquor in SIDS victims (n=27). The levels were compared with control infants dying from other causes than SIDS (n=12).

BEI measurements in CSF revealed two distinct subpopulations of SIDS, P<0.01, (G1 and G2). In approximately half of the SIDS victims (G1) there was a high level of BEI in CSF (160-400 fmol/ml CSF) and a non detectable level of BEI in ncl. tractus solitarius area (<4.3 fmol/mg tissue), p<0.05, G1 compared to G2. G1 cases had a higher level of astrogliosis in ncl. Oliva inf., p<0.01, than G2 patients. The BEI level in CSF of G1 correlated with HX concentrations in corpus vitreum liquor, r=0.92, p<0.001. The other half of SIDS cases (G2) had non detectable level of BEI in CSF (<4.3 fmol/ml) and high level of BEI in ncl. tractus solitarius area, (<4.3-17.1 fmol/mg tissue). The controls with high beta-endorphin level in CSF died under stressfull circumstances as heart operation and the controls dying from infection had low BEI in CSF.

Conclusion: SIDS is characterized by 2 groups. G1: High BEI level in CSF, low level BEI in ncl. tractus solitarius area, increased level of brainstem gliosis and a correlation between BEI level in CSF and HX level in corpus vitreum liquor. Group 2: Low BEI in CSF, high level BEI in ncl tractus solitarius area and low level of brainstem gliosis.

CIRCULATION AND HEMATOLOGY

27

DEVELOPMENTAL DIFFERENCES IN THE REAL TIME CALCIUM TRANSIENT FOLLOWING ELECTRICAL DEPOLARIZATION IN SINGLE CARDIAC MYOCYTES. Stephen Cyran, Susan Ditty, Barry Baylen, Joseph Cheung, Katheryn LaNoue, M.S. Hershey Med. Ctr., Depts. of Pediatrics and Physiology, Hershey, Pa, USA.

We previously reported developmental differences in cytosolic free calcium ($[Ca_i]$) following steady state, potassium depolarization. This study examines dynamic $[Ca_i]$ changes-$[Ca_i]$ transient:$[Ca_i]_t$-following electrical depolarization in Immature(I)/Mature(M) single cardiac myocytes via Fura-2 fluorescence. Subanalysis of $[Ca_i]_t$ into upstroke:(+)d$[Ca_i]$/dt, peak $[Ca_i]$, and downstroke (-)d$[Ca_i]$/dt was performed in the presence (+) or absence (-) of Isoproterenol(ISO).

Results (ANOVA) (*p<0.05 vs. M).

	BASE $[Ca_i]$ (nM)	PEAK $[Ca_i]$ (nM)	(+)d$[Ca_i]$/dt (nM/sec)	(-)d$[Ca_i]$/dt (nM/sec)
(-)ISO				
I	119±3*	464±11*	4094±736*	(-)582±154*
M	196±7	836±97	10650±588	(-)964±75
(+)ISO				
I	99±1	290±7*	3300±189*	(-)444±13*
M	95±3	1259±88	18740±3650	(-)2610±506

Peak $[Ca_i]$ differed between groups at rest and following ISO as did (+) and (-)d$[Ca_i]$/dt which were slower in the immature cell. Mature peak $[Ca_i]$, (+)d$[Ca_i]$/dt and (-)d$[Ca_i]$/dt increased by 50-270% in (+)ISO while immature values decreased by up to 50%. These decreases correlated with diminished real time measures of myocyte function (% shortening) in (I) and have implications regarding the effects of inotropic agents at different stages of maturation.

28

LONGITUDINAL EVALUATION OF FETAL CARDIAC GROWTH AND VENTRICULAR COMPLIANCE IN WELL CONTROLLED DIABETIC MOTHERS. Howard S Weber•, John J Botti••, Peter H Cherouny•• & Barry G Baylen•. Depts. of Pediatrics• & Perinatalogy••,Penn State University, Milton S Hershey Med Center, Hershey, PA,USA

Hypertrophic cardiomyopathy & abnormal ventricular compliance (VC) in the infant of the diabetic mother is related to poor maternal glycemic control. We prospectively evaluated cardiac growth, VC, & somatic growth in 11 normal (N) & 8 nongestational insulin dependent diabetic (D) pregnancies using fetal echo from mid gestation to term. Studies were performed at gestational age (GA) P1) 20-26 wks; P2) 27-33 wks; P3) 34-40 wks & P4) 48-72 hrs postnatally. Septal (S) wall thickness (mm) in diastole was obtained using M-mode echo (4 chamber view). Indices of right & left VC were obtained from diastolic tricuspid & mitral E & A wave time velocity integral ratios (TVIE/A, MVIE/A). Weight (W) in grams was estimated from biparietal diameter & abdominal circumference. Glycemic control was measured from % glycosylated hemoglobin (A1C). Placental resistance was evaluated by the Pulsatility Index (PI) from umbilical artery flow. Values are expressed as the mean ± 1 SD.

	W	S	TVIE/A	MVIE/A	A1C	PI	GA
P1(N)	434±73	2.7±.4	.62±.09	.65±.08	4.3±1.0	1.3±.3	21.5±1.2
P1(D)	490±83	2.9±.6	.71±.17	.70±.11	4.5±0.7	1.5±.3	22.3±1.3
P2(N)	1404±188	4.1±.4	.71±.13	.82±.10	4.0±0.3	1.2±.1	30.0±0.6
P2(D)	1613±296	4.5±.6	.66±.13	.71±.16	4.7±0.8	1.1±.2	30.1±0.6
P3(N)	2280±368	4.7±.8	.80±.17	.90±.17††	4.1±0.3	1.0±.2	35.5±0.9
P3(D)	2901±352	5.3±.8	.84±.18	.74±.22	4.5±0.1	1.0±.2	35.8±0.5
P4(N)	3482±464	5.0±.5*	.90±.29†	1.36±.34*	3.3±0.3		64±25
P4(D)	3760±589	5.4±.7*	.76±.19	1.26±.36*	3.8±0.4		67±19

Both N & D demonstrated increased left VC & S from P1 to P4 (*p<.01,ANOVA) while right VC increased in N only (†p<.01,ANOVA). In N, left VC increased earlier (P1 to P3, †† p<.01,ANOVA). All variables between N & D within each period were similar (p>.05, t-test). Thus glycemic control (A1C) in D results postnatally in normal cardiac growth, birth weight & VC in comparison to N although right & left VC does not progress normally.