

THE EFFECT OF EUGLYCEMIC HYPERINSULINEMIA ON CEREBRAL GLUCOSE METABOLISM IN NEWBORN BEAGLES. C Trindade, M Huang, S Hulman, S Reef, RM Kliegman. Case Western Reserve Univ, Dept Peds, Cleve, OH

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The role of insulin (IN) on cerebral glucose (glu) metabolism in newborn mammals is unknown. We employed the euglycemic hyperinsulinemic (HI) clamp (N=36) alone or combined with tissue 2-deoxy [¹⁴C] glucose (2DG) uptake (N=21) to see the effects of HI (33-14,333 uU/ml) on cerebral metabolites and 2DG uptake. Control (N=14) vs HI, basal glu (3.1±1.4 v 3.7±1.1 mM) basal glu utilization (33±8 v 31±12 umol/kg/min) were similar. During HI, glu levels did not change (3.7 v 3.8 mM), however glu utilization increased to 54±28, p<0.005. Compared to fasting values brain metabolites were not changed by HI: glu (1.7±0.9 v 2.0±1.0 umol/g), UDP-glu (0.067±0.026 v 0.069±0.035), glycogen (0.92±0.47 v 1.1±0.69), pyruvate (0.12±0.05 v 0.12±0.05), lactate (0.99±0.52 v 0.93±0.41), citrate (0.21±0.05 v 0.21±0.08). Furthermore, glu-6-P, fructose-6-P, phosphoenolpyruvate alanine, glutamine glutamate, aspartate and ATP were not different. The uptake of 2DG was analyzed as a function of plasma insulin levels (120-6000uU/ml) in brain and also compared with more insulin sensitive tissues; muscle and liver: Mean±S.D.

	Uptake dpm/g/min	r vs insulin level	p value
Brain	203±192 (33-713)	0.56	<0.05
Liver	468±391 (102-1611)	0.75	<0.001
Muscle	63±51 (20-218)	0.62	<0.01

Conclusion: Although HI did not affect brain metabolites, there was a significant dose response of brain 2DG uptake as a function of increasing insulin levels. Neonatal canine brain may be an insulin sensitive tissue.

COMPARISON OF POSTPRANDIAL FOREARM vs CALF BLOOD FLOW CHANGES IN PRETERM AND TERM INFANTS. Gloria Valencia, Patricia Frankfort, Adela Gatnaitan and Alice C. Yao. Dept. of Pediatrics, SUNY Health Science Center, Brooklyn, New York.

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Calf blood flow (CBF) in term infants has previously been found to respond to feeding by an initial decrease followed by a postprandial hyperemia. In contrast, preterm infants showed this regional redistribution only when their postconceptual age approached term. The purpose of this study was to find out whether CBF is a uniform reflection of the infant's peripheral circulation.

Postprandial CBF and forearm blood flow (FBF) were measured in 9 term (>37 wks. g.a.) and 6 preterm infants by venous occlusion plethysmography. Peripheral vascular resistance (PVR) was calculated from mean blood pressure and limb blood flow (LBF).

Postprandial FBF paralleled the changes in CBF i.e., an initial decrease followed by an increase in seven out of nine term infants, but only in two out of six preterm infants. In four of the six preterm infants FBF did not follow changes in CBF. In three of them FBF decreased 15-30 minutes after feeding, and subsequently increased, similar to term infants. PVR varied indirectly with LBF.

It is suggested that in term infants, postprandial FBF changes were more consistently in accordance with CBF changes than in preterm infants. (YAO et al, Colloque INSERM 133:177, 1986.)

PLASMA ATRIAL NATRIURETIC PEPTIDE HORMONE (ANH) LEVELS IN HEALTHY FULL TERM (FT), HEALTHY PREMATURE (HP) AND SICK PREMATURE (SP) INFANTS. Carmen L. Villaveces, Larry Barak, Allen Root, Keith S. Kanarek, Greg Duckett, U.S.F. College of Medicine, Department of Pediatrics, Tampa, Florida.

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Plasma ANH levels (pg/ml) were measured in 13 FT, 9 HP and in 11 SP infants with respiratory distress syndrome (RDS). The mean ± SD gestational age (GA), birth weight (BW), and plasma values from cord blood and at 24 hours, 48 hours and 8 days are shown in the Table.

	FT	HP	SP
GA(wks)	40.1	33.78±1.	29.4±2.1
BW(gms)	3412.5	1688.8±419.4	1112.3±339.7
Cord	153.4±23.3	107.1±63.6	
24 hour	213.0±120.4	133.2±72.4	98.0±42.4
48 hour	272.8±84.8*	676.1±682.1*	112.6±98.0**
8 day		117.5±81.2	272.9±523

* and ** p<0.05

In F.T. and H.P. infants plasma ANH levels increased significantly 48 hrs after birth. The plasma ANH levels in the S.P. infants at 48 hrs was significantly lower than in the H.P. infants (P<0.05). Failure of the ANH values to increase at 48 hrs of age in S.P. infants with R.D.S. may be partially responsible for the failure of a diuresis characteristic of infants with RDS at this age.

COORDINATE ACTIVATION OF THE DOLICHO-LINKED PATHWAY TO GLYCOPROTEINS IN DEVELOPING BRAIN. Joseph J. Volpe, Yoichi Sakakihara and Robert S. Rust. Washington University School of Medicine, St. Louis Children's Hospital, Departments of Pediatrics, Neurology, Biological Chemistry, St. Louis, MO.

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Glycoproteins play critical roles in brain development, including particularly neuronal and glial differentiation. However, little is known about the regulation of glycoprotein synthesis in developing brain. Glycoprotein biosynthesis is known to occur via the dolichol-linked pathway, in which dolichyl phosphate (dol-P) is the critical intermediate. In this work we utilized developing rat brain to study the regulation of dolichol-linked glycoprotein biosynthesis. Utilization of a new technique based upon high performance liquid chromatography led to the definition of a striking increase in brain content of dol-P in the 2nd to 4th weeks of postnatal development. Values increased 10-fold from 10 days of life to 25 days of life. Strikingly, specific activity of dolichol kinase, the enzyme that catalyzes formation of dol-P from dolichol and cytidine triphosphate, exhibited a parallel developmental increase. Similarly, the specific activity of the first committed enzyme in the transfer of saccharide moieties to dol-P, the tunicamycin-sensitive N-acetylglucosaminylphosphotransferase, also exhibited a sharp developmental increase in the 2nd to 4th weeks. Taken together the data indicate for the first time that dolichol kinase is the critical determinant of dol-P levels in brain, and that coordinate activation of the dolichol-linked pathway to glycoproteins occurs at a developmental time period which includes neuronal and glial differentiation. (Supported by NIH-R01-HD07464).

THE PROSTACYCLIN ANALOG CARBACYCLIN CROSSES THE PLACENTA IN AN IN VITRO PLACENTAL PERFUSION MODEL. R. W. Walenga, D. Kuhn, and M.J. Stuart, SUNY, Health Science Center, Dept. of Pediatrics, Syracuse, N.Y.

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Prostacyclin has been proposed as therapy in pathological states associated with placental insufficiency. It is important therefore to determine whether this compound, and agents with similar structures and effects, cross the placenta, affecting the fetus. We have developed a method for the assay of carbacyclin (6-carba-prostacyclin) in fetal effluent in an in vitro placental perfusion model. Prostaglandin B₂ (PGB₂) is added as internal standard at 1.0µM and samples (or standards in fetal effluent) were subjected to solid phase extraction and reverse phase HPLC using acetonitrile-0.1% acetic acid as the mobile phase. The fractions containing PGB₂ and carbacyclin were sequentially derivatized with ethereal diazomethane and BSTFA to yield methyl ester-trimethyl silyl ethers. These were separated by capillary gas chromatography and monitored in a mass selective detector. For the PGB₂ peak, mass fragments of m/z=420 and 321 were monitored, and for carbacyclin 418, and 321. Concentration of carbacyclin in experimental samples was calculated from standard curves of area ratio vs mass ratio. In the in vitro perfused placenta, when carbacyclin was added only to the maternal afferent circulation, it was detected in the fetal effluent. When maternal afferent contained 1.0µM carbacyclin, fetal effluent reached a concentration of 0.18µM within 20 minutes; when the maternal afferent contained 10µM, the fetal effluent reached 0.66µM. Thus carbacyclin crosses the placenta, and while the transfer does not appear to concentrate that agent, sufficient levels are reached to produce physiological responses.

LEFT PULMONARY ARTERY (LPA) LIGATION IMPAIRS FETAL LUNG GROWTH. Linda D Wallen, Colleen S Kondo, Yoshimi Takahashi, John E Maloney (Spon by D. Grant Gall).

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Pulmonary hypoplasia is a common cause of neonatal respiratory disease. Despite evidence in humans that normal fetal lung growth depends on pulmonary arterial flow, this relationship has not been investigated. To determine whether pulmonary arterial flow is necessary for lung growth, the LPA was ligated in 5 fetal sheep during the canalicular stage of lung development (105-114d gestation). Lung growth at 140d gestation was compared to 4 sham operated (105-114d) and 5 term (139-144d) control fetuses. Fetal lungs were prepared for morphologic and morphometric analysis. LPA ligation markedly reduced all left lung weights and the amount of parenchymal tissue compared to both sham and control groups. Fetal surgery significantly reduced sham left lung weights compared to control, and LPA ligated and sham right lung weights compared to control (Table). Thus, pulmonary arterial flow is essential for normal lung growth. Investigation of causes of pulmonary hypoplasia should include consideration of pulmonary arterial flow, and unoperated controls should be used to evaluate normal lung growth.

	LPA LIGATED	SHAM OPERATED	TERM CONTROLS
Left Wt. (g)	28 (10)**	50 (10)+	85 (18)
Wt. (% body wt.)	0.6 (0.2)**	1.2 (0.2)+	1.8 (0.4)
Dry wt. (g)	3.5 (1.2)**	6.5 (1.0)+	9.4 (2.6)
Right Wt. (g)	103 (25)+	85 (10)+	138 (22)
Wt. (% body wt.)	2.2 (0.4)+	2.1 (0.3)+	3.0 (0.4)
Dry wt. (g)	12.1 (3.0)	10.3 (1.1)	14.4 (1.9)

All values mean (SD). + P<0.05 vs controls. *P<0.05 vs sham.