NEUROLOGY

●1657 MAGNETIC RESONANCE (MR) BRAIN IMAGING IN GENETIC METABOLIC DISEASES: DIAGNOSTIC AND THERAPEUTIC IMPLICATIONS. Richard J. Allen, Steven Gebarski, and Alex Aisen, University of Michigan Medical School, Mott Children's Hospital, Section of Pediatric Neurology and Neuroradiology, Departments of Pediatrics, Neurology, and Radiology, Ann Arbor, MI.

CNS "damage" in certain genetic metabolic diseases is recognized in part by neuropathological abnormalities in non-survivors. One universal characteristic in infants is spongy demyelination (SDI) of cerebral white matter (myelin). The relationship to specific biochemical events is unknown. Hydrogen proton MR sensitive to changes in myelin signal (MRS) is a non-invasive technique highly applicable to the in-vivo study of dysmyelination at all ages. Preliminary studies in several metabolic disorders with/without therapy (Tx) at different ages demonstrates:

Disorder	Pt's	Age	Results (↓↓ MRS)
PKU	4	8m,1y,17y,32y	Normal(with/without Tx)
MSUD	3	3m,8y,14y	Generalized ↓ (↓with Tx)
Homocystinuria	1	15y	Normal
Nonketotic-Hyperglycinemia	1	8m	Generalized ↓
Propionic-Acidemia	1	21y	Normal (after Tx)
Mitochondrial-lacticacidemia	2	5y,16y	Localized striatal ↓

MR performed on a superconducting .35 Tesla unit with spin echo technique, spin-spin relaxation time (T_2) weighted imaging sequences (repetition time TR), 2000 msec.: echo time (TE) 56 ms, proved most sensitive. These MR findings provide a better understanding of metabolic dysmyelination and the therapeutic CNS response.

1658 TROPHIC LIMB CHANGES FOLLOWING EARLY UNILATERAL BRAIN INSULT. D.M. Aram, B.L. Ekelman, P. Satz (Spon. by R.J. Martin), Case Western Reserve University, Dept. Ped., Cleveland; UCLA, Dept. of Psychiatry, Los Angeles.

Trophic limb changes following early unilateral brain lesions have been noted clinically for years. No studies, however, have reported foot and hand length of children with CT scan verified lesions of known age of onset. Measurements of foot and hand length for 15 neurologically normal, 17 L brain lesioned, and 12 R brain lesioned young children were taken >2 yrs. post lesion onset. Results are as follows:

	LEFT-LESIONED	RIGHT-LESIONED	NORMALS
FOOT LENGTH	R<L; t=-3.31; p<.01	R>L; t=3.73; p<.01	R=L; t=-1.85; NS
HAND LENGTH	R<L; t=-6.11; p<.001	R>L; t=3.65; p<.01	R=L; t=.81; NS

Direct comparisons of foot and hand asymmetry for L and R lesioned children also are highly significant:

MEASUREMENT:	FOOT		HAND		
	R>L	R<L	R>L	R<L	R=L
L LESIONED (N=17)	2	15	1	15	1
R LESIONED (N=12)	11	1	11	0	1
	x^2=15.07; p<.001		x^2=23.16; p<.001		

When a >.2 cm cut-off level in foot asymmetry is established, 9 of the 12 R lesioned children, 11 of the 17 L lesioned children, and only 1 of the 15 normal children are identified (chi square= 12.98; p<.001). Further, all but 1 of the 11 L brain lesioned subjects with >.2 cm difference is L handed. These findings suggest that asymmetric foot and hand development may provide a subtle biological marker for early CNS pathology among children who otherwise are neurologically asymptomatic and may signal pathological L handedness.

1659 MURINE CYTOMEGALOVIRUS INFECTION OF FETAL BRAIN AGGREGATES. James F. Bale, Jr., Marsha O'Neil, and Robert Schelper (Spon. by FG Smith, Jr.), University of Iowa College of Medicine, Departments of Pediatrics, Neurology and Pathology, Iowa City, Iowa.

Human cytomegalovirus (CMV) infection can severely damage the developing nervous system and cause major neuropathologic abnormalities including cerebral necrosis, cerebral calcification and defects in neuronal migration. To study CMV infection of developing neural tissues, we infected fetal mouse brain cell cultures in vitro with the Smith strain of murine CMV (MCMV). Aggregating brain cell cultures were prepared from late-term fetal mice and after 21 to 28 days in culture were inoculated with 1.0 plaque-forming unit (pfu) of MCMV per 10^3 viable cells. MCMV could be recovered from culture fluids 1, 3, 5, 7 and 14 days after infection, and titers of MCMV rose steadily: mean of 4.0 pfu of MCMV/ml of culture fluid on day 1, 6.7 x 10^1 pfu of MCMV/ml on day 3, 4.3 x 10^3 pfu of MCMV/ml on day 5 and 7.6 x 10^3 pfu of MCMV/ml on day 7. Assay of washed brain aggregates 7 days after infection yielded 4.6 x 10^2 pfu of MCMV per aggregate, and immunofluorescence staining confirmed the presence of MCMV antigens. Electron microscopic studies of MCMV-infected aggregates demonstrated intranuclear inclusions and numerous intranuclear and intracytoplasmic virus particles in neurons, astrocytes and oligodendrocytes. These results indicate that MCMV replicates in fetal mouse brain aggregates and produces ultrastructural changes typical of CMV infections. These studies provide an in vitro method by which to investigate the effects of CMV infection on developing neural tissues.

†1660 THE SPECTRUM OF SONOGRAPHIC FINDINGS IN FULLTERM (FT) ASPHYXIA. J. Barks, J. Hellmann, A. Daneman (Spon. by P.R. Swyer). Depts. Pediatrics and Radiology, Hospital for Sick Children, Toronto, Canada.

Cranial ultrasound (US) has not been considered useful in the assessment of FT asphyxia. 31 infants with at least 2 of the following were evaluated: fetal distress, Apgar ≤5 at 1 or 5 min, need for immediate resuscitation and abnormal neurological examination in 1st 24 hrs. One infant with only latter finding was included. All infants had at least 1 US in 1st 7 days. US revealed 2 major patterns of abnormality, diffuse and focal. The severity of asphyxia was graded by clinical and EEG criteria.

Severity	A.Mild(10)	B.Moderate(13)	C.Severe(9)
Apgar (Median)	3.5/6	3/6.5	3/3
US - Normal	9	9	4
Diffuse	0	3	3
Focal	1	1	3
Other	0	2	2
CT correlation	1/2	5/6	4/6

In B & C 7/13 normal US were done on day 1 or 2 and 4/13 with only small ventricles were graded normal. Diffuse changes with slit-like ventricles and loss of anatomic landmarks or diffuse ↑ in echogenicity were seen in 6 infants. Focal ↑ in echogenicity was cortical in 2 infants and in periventricular white matter in 3. US did not reveal a frontal cortical hemorrhage and 2 MCA infarcts diagnosed on CT 1 & 4 days later. The usefulness of US in FT asphyxia can be improved by repeating early normal studies if moderate or severe clinical abnormalities persist.

†1661 ESTIMATION OF CEREBRAL BLOOD FLOW BY DOPPLER Keith Barrington, Donald Boisvert, Kenneth Hutchison, Michael Nosko (Spons. by Neil Finer). University of Alberta, Departments of Pediatrics, Neurosurgery, and Physiology, Edmonton, Alberta, CANADA

In an effort to determine the accuracy of range-gated Doppler ultrasound (DUS), we compared measures of flow through the exposed carotid artery of 6 anesthetized adult female cynomolgus monkeys using DUS (20 MHz) with those obtained using an electromagnetic flow (EMF) probe and direct measures of cerebral blood flow (CBF) using Xe 133 clearance. Vessel calibre was determined by calibrated angiography. A fast fourier transform was performed every 6.25 milliseconds on the DUS shifted spectra and averaged over 15 cardiac cycles. Mean flow velocity was derived and multiplied by vessel cross-sectional area to give volumic flow. Variations in CBF were produced by altering $PaCO_2$. Pulsatility index (PI) was calculated from the output derived from a zero-crosser incorporated into the DUS device. Twenty-one comparisons were performed over a wide range of CBF (17 to 96 ml/100 gm/min). Correlation between Xe 133 and DUS volumic flow measurements was highly significant, r = 0.8, p <.0001). The correlation between Xe 133 and flow velocity, without correcting for vessel diameter, was poorer (r = 0.7, p <.0002) as was the correlation between DUS & EMF (r = .51, p <.05). The correlation between EMF & Xe 133 (r = .7, p <.0004) was lower than that between DUS & Xe. Even under these ideal conditions, PI did not correlate with CBF. This method for estimating CBF does not involve ionizing radiation and could be adapted to produce a totally non-invasive methodology for measuring CBF in real time.

†1662 EARLY VENTRICULOPERITONEAL (VP) SHUNTS IN INFANTS WEIGHING 2000 GM: NEURODEVELOPMENTAL FOLLOW-UP. Carole A. Boynton, Bruce R. Boynton, T.Allen Merritt, Yvonne E. Vaucher, Hector E. James and Raul F. Bejar. UCSD School of Medicine, San Diego; Departments of Pediatrics and Surgery.

The optimum time for VP shunt placement in infants with post-hemorrhagic hydrocephalus is controversial. We studied 28 preterm infants born between 1979-1983 (mean birthweight 1338±329gm; mean gestational age 30±2wk) in whom serial lumbar punctures failed to control progressive and symptomatic ventriculomegaly after grade III (62%) or grade IV (38%) intraventricular hemorrhage. VP shunts were placed at a median age of 28 days (range 11-78 days). Seventeen infants (61%) required 1 or more shunt revisions and 10(36%) had shunt infections. Three infants died, 1 from a shunt infection. The infants were evaluated with audiologic, ophthalmologic and neurologic examinations. Eight infants (29%) have profound visual loss, 5 of whom have cortical blindness, and 7 (25%) have hearing impairment. Five infants have profound neurological sequelae and 7 have seizure disorders. A developmental quotient (DQ) and motor index (MI) were obtained between 4-12 months adjusted age using the Bayley and/or Knobloch-Gesell scales. The number of infants having various developmental scores is shown below:

SCORES	≤ 50	51-84	≥85	Range	Mean
DQ	13	5	7	89-120	100.9
MI	13	6	6	86-110	96.0
DQ & MI	12	2	5		

Although nearly 20% of these infants have normal DQ&MI at 1 year of age, progressive posthemorrhagic hydrocephalus is associated with multiple handicaps despite early VP shunt placement.
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