Common Neonatal Lesions

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Neuro MRI Course May 11th 2011

Introduction

- Common Lesions in the Term Infant
  - What is currently done in clinical practice
  - Significance of Cerebral Lesions
- Common Lesions in the Preterm Infant
  - Prognostic Significance of the lesions

The most important ingredient..

- Good communication between the clinical and radiological team
  - The clinical details of the infant and likely diagnoses – what the question is for the imaging? (clinician)
  - What to order? (radiology)
  - What is present in the images (radiology)
  - Prognosis and follow up (clinician)

This can be met with regular co-review of the images (daily, weekly meeting) and also quarterly- annual review of the numbers of infants imaged, diagnoses, schema for imaging etc

The term infant

What imaging is done in term infants?

- 88,527 infants screened from 70 Centers
  - All Centers had access to MR Imaging
- 1,743 (2%) met criteria for encephalopathy
  - 34 (2%) infants had evidence of cerebral dysgenesis on neuroimaging and excluded
- 1,421 (82%) underwent some form of neuroimaging evaluation
  - Of the 322 (18%) of infants that did not have any neuroimaging there were 62 deaths (30 on day 1 and 61 by day 7)
  - 15% living term NE infants NO neuroimaging

Results

		Ultrasound	CT Scan	MRI
Number of exams		**729 (51%) 42% total**	**477 (34%) 28% total**	**1074 (75%) 63% total**
Mean (SD) age (days) at first exam		**3.1 (4.4)**	**3.2 (3.5)**	**7.3 (8.7)**
Abnormal				
Hemorrhage	IVH/SE			
	Extra-axial			
	Parenchymal			
DNGM				
WM Injury				

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Hemorrhage	IVH/SE	56 (8%)	59 (12%)	79 (7%)
	Extra-axial	24 (3%)	165 (35%)	212 (20%)
	Parenchymal	37 (5%)	57 (12%)	105 (10%)
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DNGM		70 (10%)	50 (10%)	309 (29%)
WM Injury		16 (2%)	15 (3%)	271 (25%)

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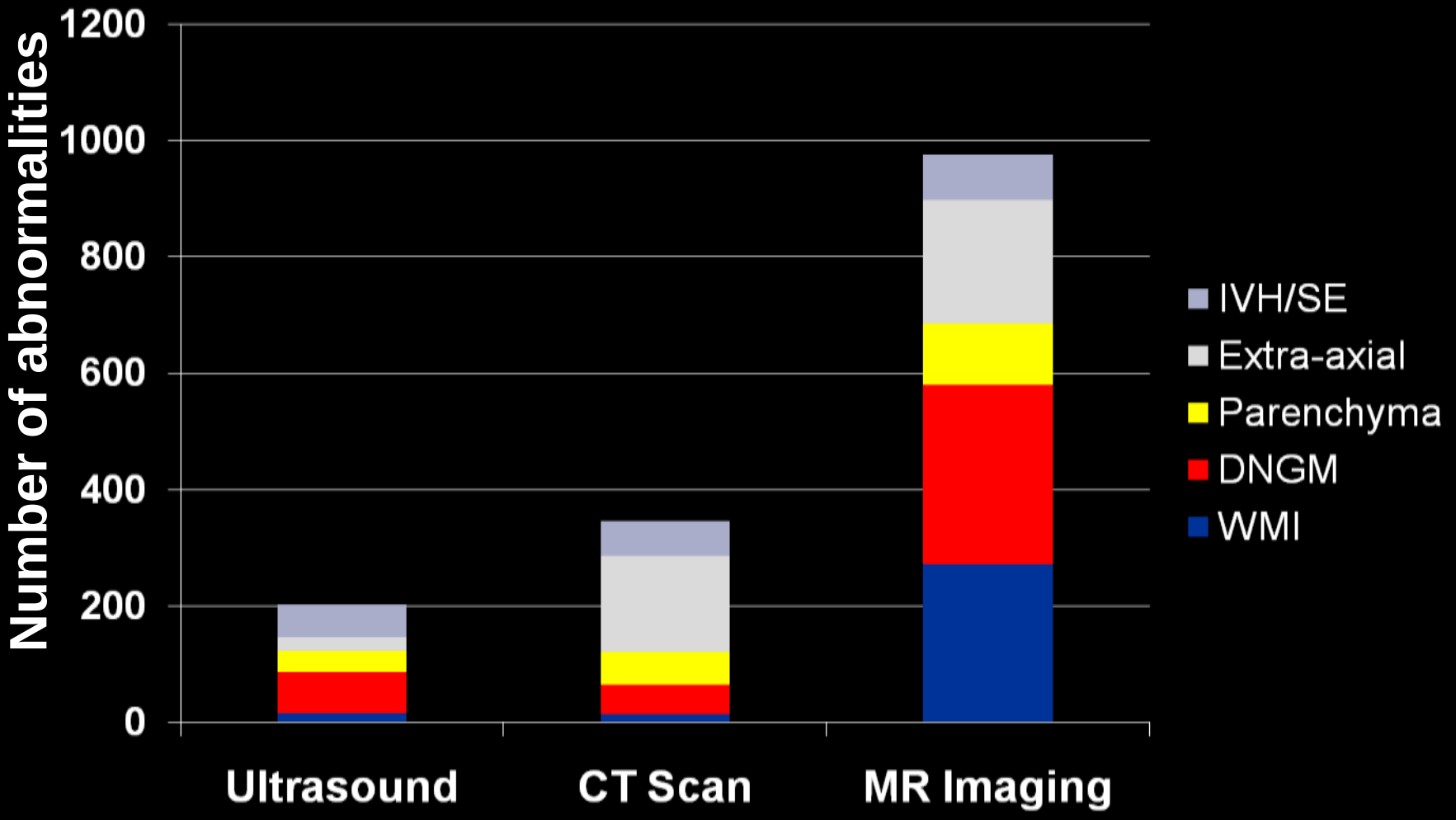
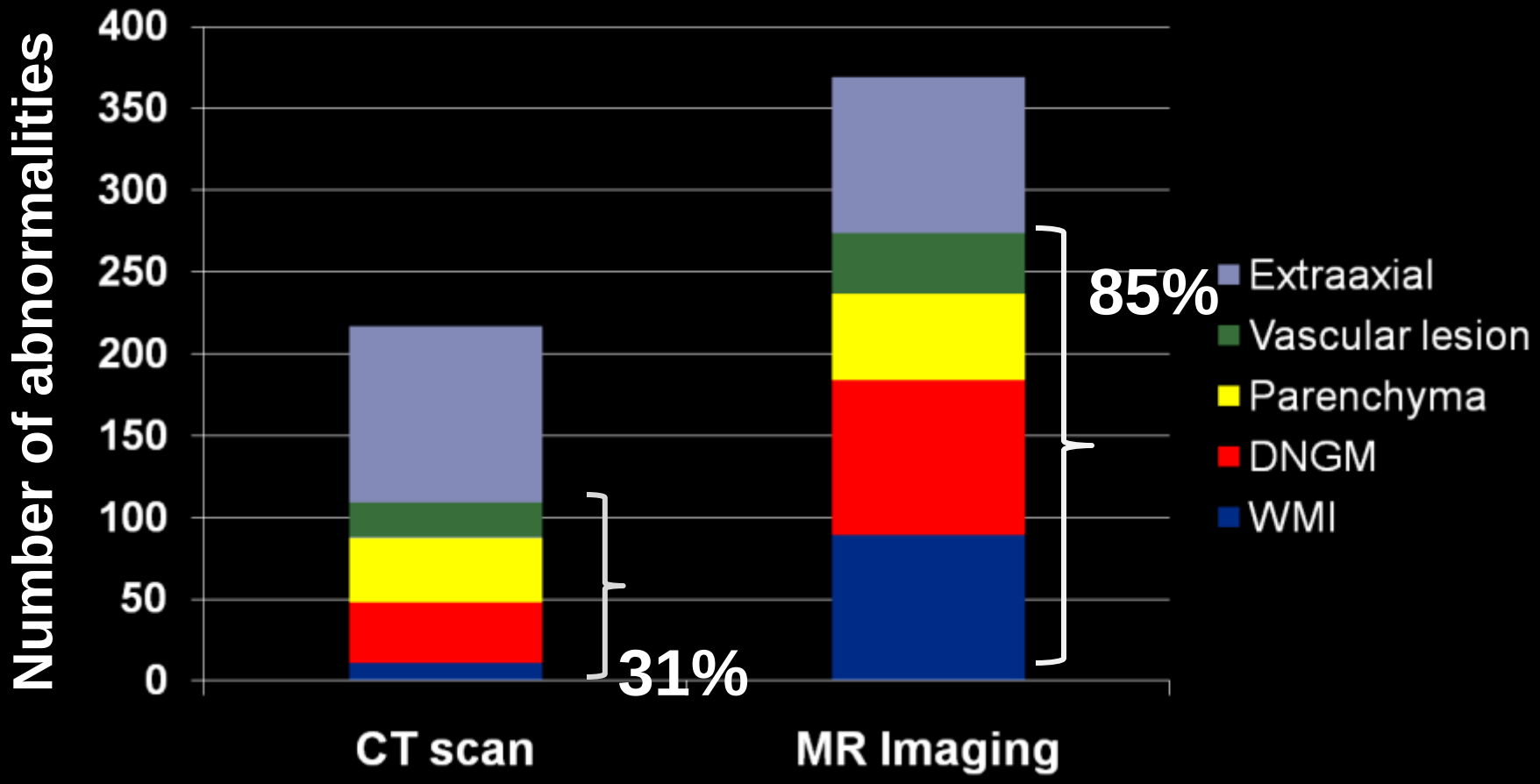
Abnormalities on Imaging



317 (20%) infants-both CT and MRI



Higher detection on MRI: WM Injury 10X, DNGM 3X, Vascular lesions 2X

Conclusions

- There is a wide variation in the use of neuroimaging in NE in term infants
- CUS and CT similar rates of significant neuropathology
- MR imaging more often revealed vascular lesions, white matter and deep nuclear gray matter injury of prognostic significance (*Chau et al Pediatrics 2009;123:319-326*)

Conclusions – Avoid CT

- Radiation from CT scans done in 2007 will cause 29,000 cancers and kill nearly 15,000 Americans.(Reuters February 2010)

- **Radiation Risks from CT in Children: A Public Health Issue (National Cancer Institute – NIH December 2008)**
- Major national and international organizations agree no amount of radiation should be considered absolutely safe.

- The benefits of CT examinations should always outweigh the risks for an individual child; unnecessary exposure is associated with unnecessary risk.
  - **http://www.cancer.gov/cancertopics/causes/radiation-risks-pediatric-CT**

Why image in the Term Encephalopathic Infant?

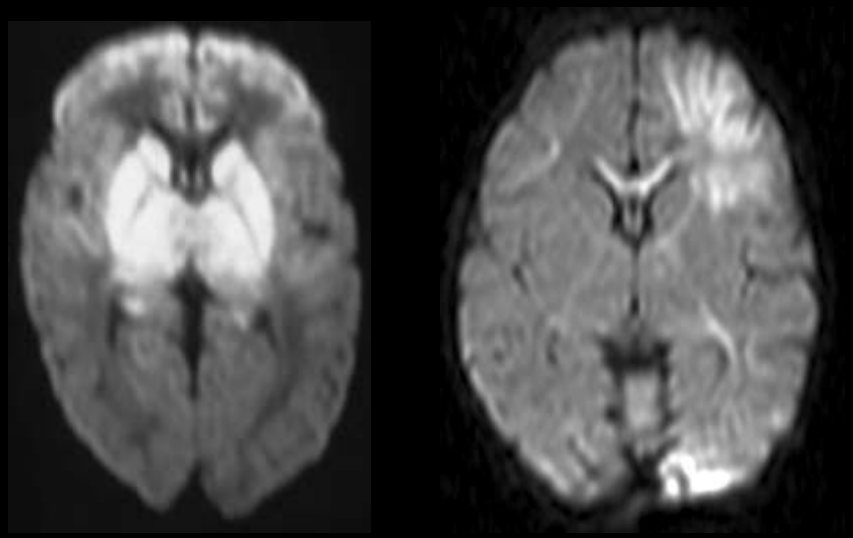
- Confirm the diagnosis
- Define the nature and the extent of injury – prognosis and early intervention services

Patterns of cerebral injury

Shalak L, Perlman JM. Early Hum Dev. 2004 Nov;80(2):125-41.

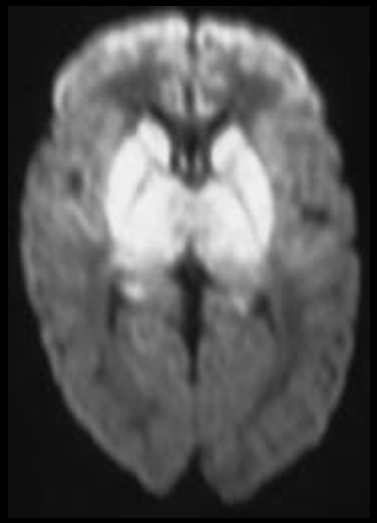
Intrapartum Hypoxic-Ischemic Brain Injury

Acute Injury
Sentinel Event
Cord pH < 7.00
Resuscitation
Low Apgar scores
Encephalopathy
Renal dysfunction
Neuroimaging +



Subacute Injury
Normal Labor
Cord pH > 7.00
Minimal resuscitation
Good Apgar scores
Encephalopathy
Neuroimaging +

Clinico-pathological correlate



Isolated basal ganglia injury

Neonatal period – hypotonia

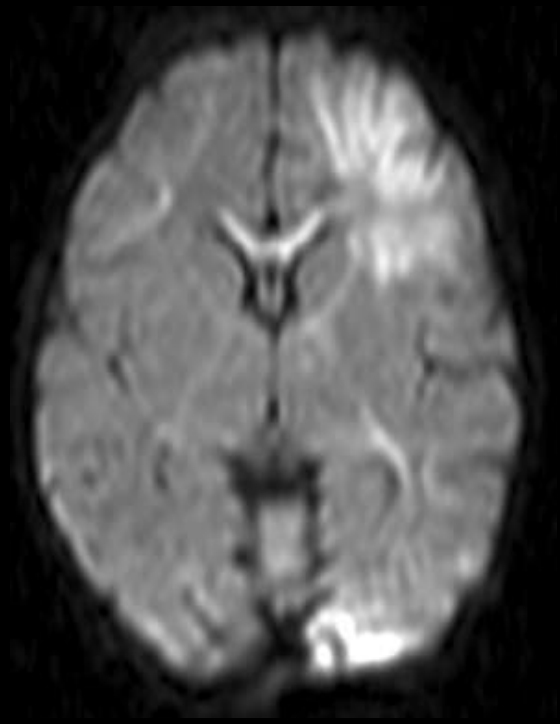
Later – High risk for adverse outcome
spastic quadriparesis, movement disorders
(may have spared intellect and language)

Clinico-pathological correlate

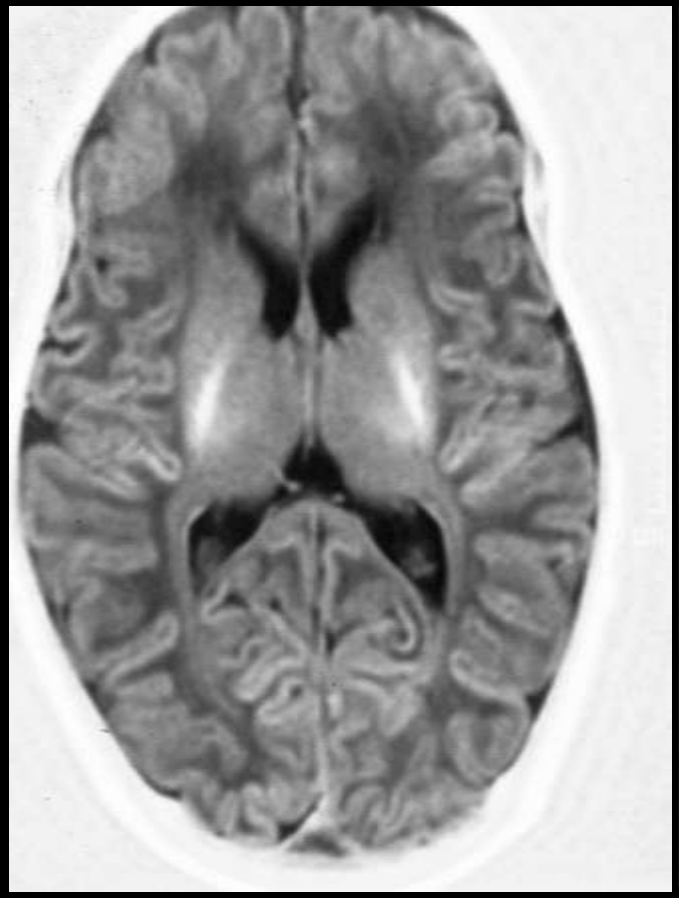
Selective cortical neuronal injury - parasagittal

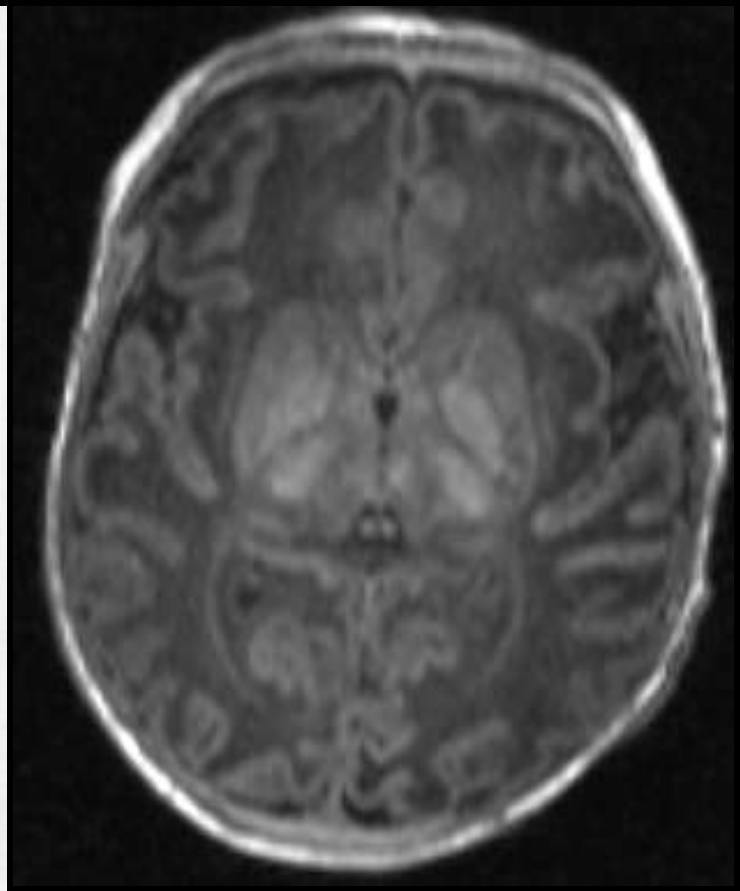
Neonatal period – proximal axial weakness

Later – Lower risk for adverse outcome
- Specific intellectual impairments including memory, visuospatial & language



Posterior Limb of the Internal Capsule



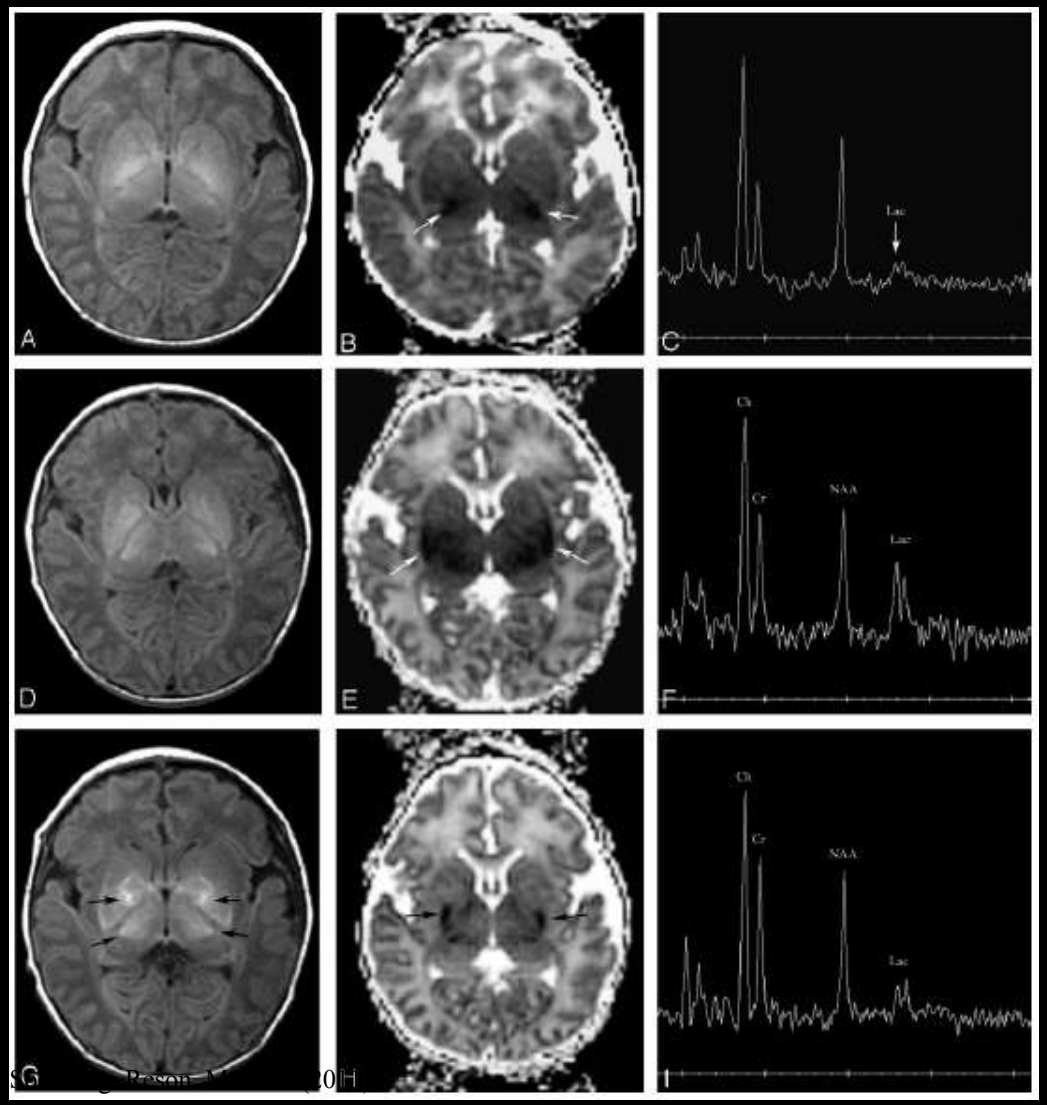


Abnormal PLIC in relation to outcome Rutherford et al; *Pediatrics 1998*

PLIC	Outcome Abnormal	Outcome Normal
Normal	0	28
Abnormal	41	4*

* these infants had extensive white matter damage; sensitivity 0.90; specificity 1; PPV 1; NPV 0.87

Evolution of Neuroimaging



16 hours

Imaging evolved
Lactate increase
Extension of DNGM

4 days

8 days

Barkovich AJ et al
AJNR 2006:27:533-47

Impact of Hypothermia

Reduction in cerebral lesions on MRI with therapeutic hypothermia (TOBY trial)

Lesion site	Adjusted odds ratio (95% confidence intervals)
Basal ganglia and thalami	0.36 (0.15-0.84) P=0.02
Posterior limb of internal capsule	0.38 (0.17-0.85) P=0.02
White matter	0.30 (0.12-0.77) P=0.01
Cortex	0.62 (0.27-1.41) P=0.25

Accuracy of prediction of outcome by MRI following therapeutic hypothermia

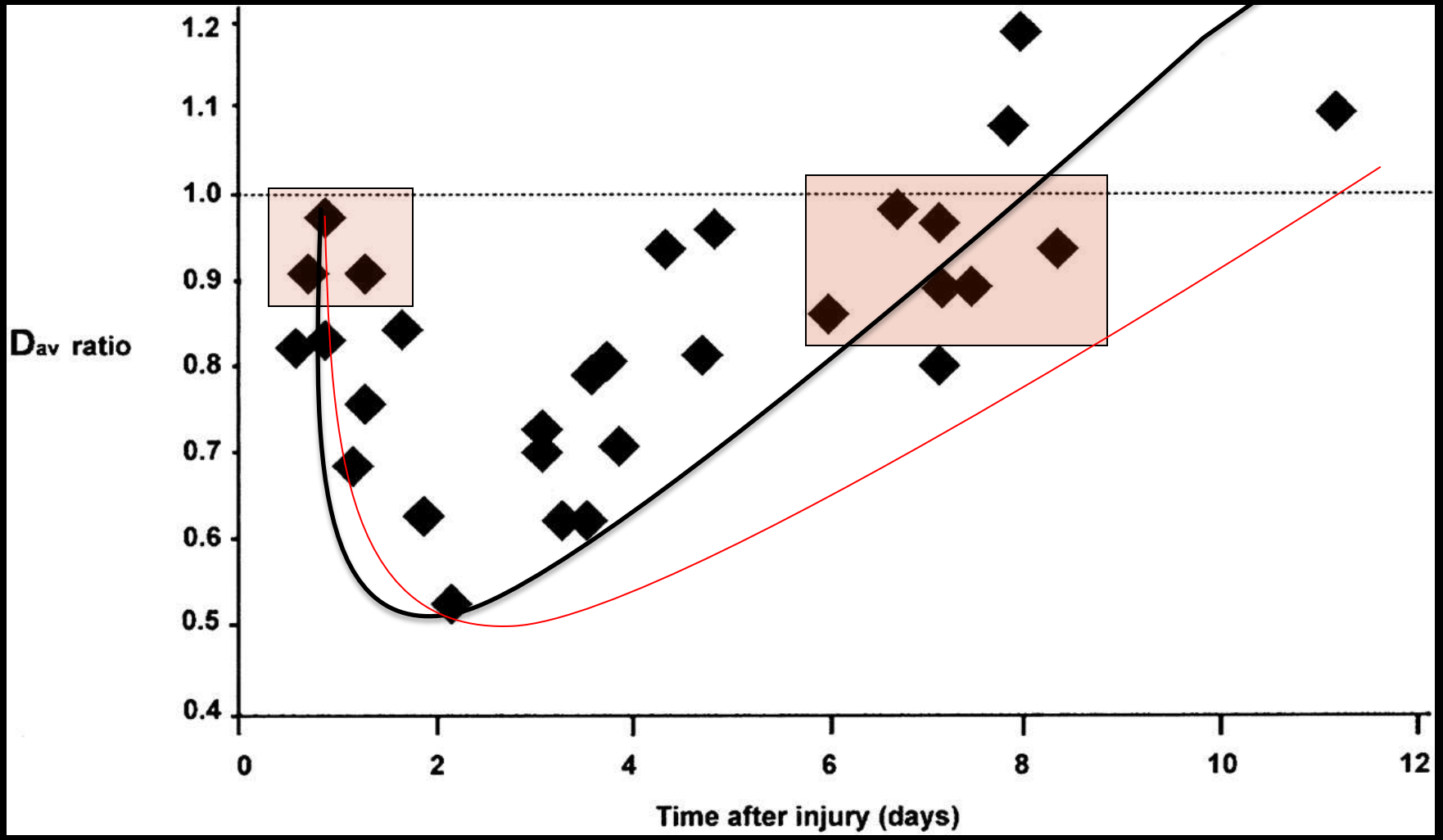
Major MRI abnormalities	Cooled(95% Confidence intervals)	Non cooled(95% Confidence intervals)
Sensitivity	0.88 (0.79-0.97)	0.94(0.88-1.0)
Specificity	0.82(0.72-0.92)	0.68(0.56-0.80)
Positive predictive value	0.76(0.65-0.87)	0.74(0.63-0.85)
Negative predictive value	0.91(0.83-0.99)	0.92(0.85-0.99)

Impact of hypothermia

Eighteen infants fullfilled the injury criteria MRI.

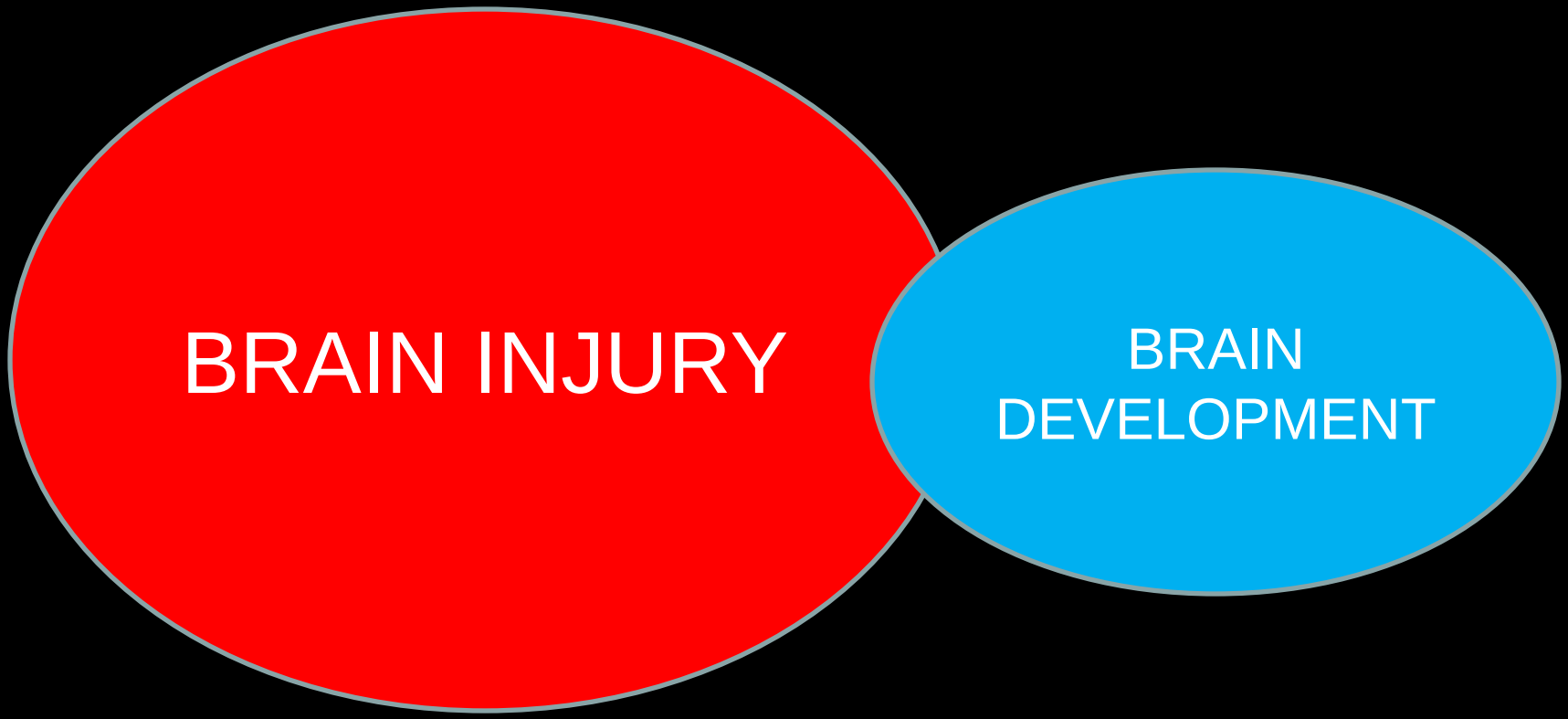
Dav values were decreased in injured infants two days after injury with a maximum decrease of 50 % than reference values.

The return to reference value (pseudonormalization) was observed to occur after the tenth day.



McKinstry RC et al.
Neurology. 2002 59:824-33.

Premature Infant

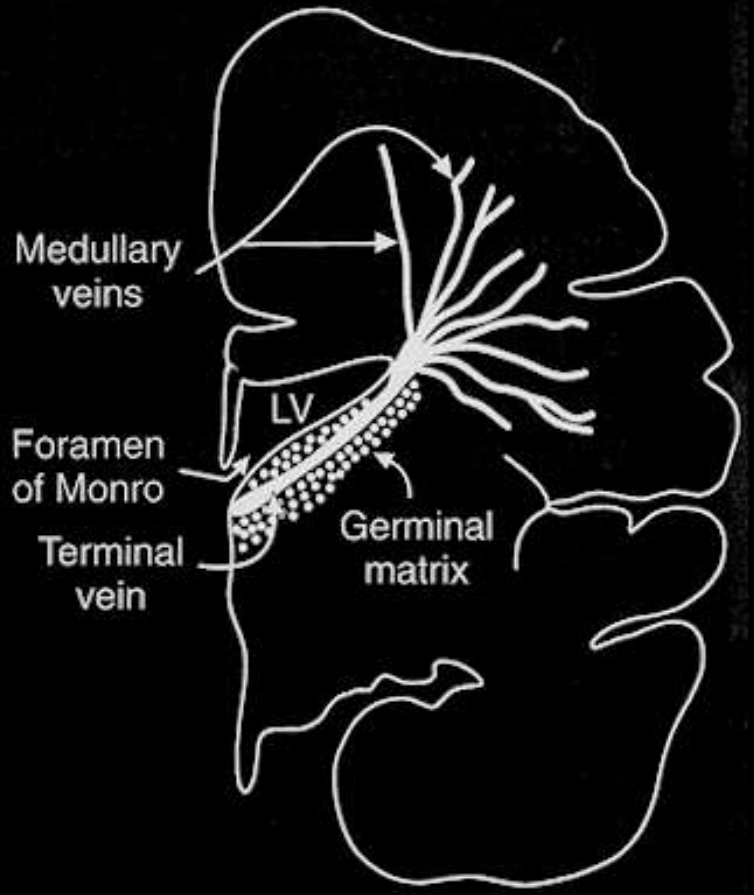

BRAIN INJURY
BRAIN
DEVELOPMENT

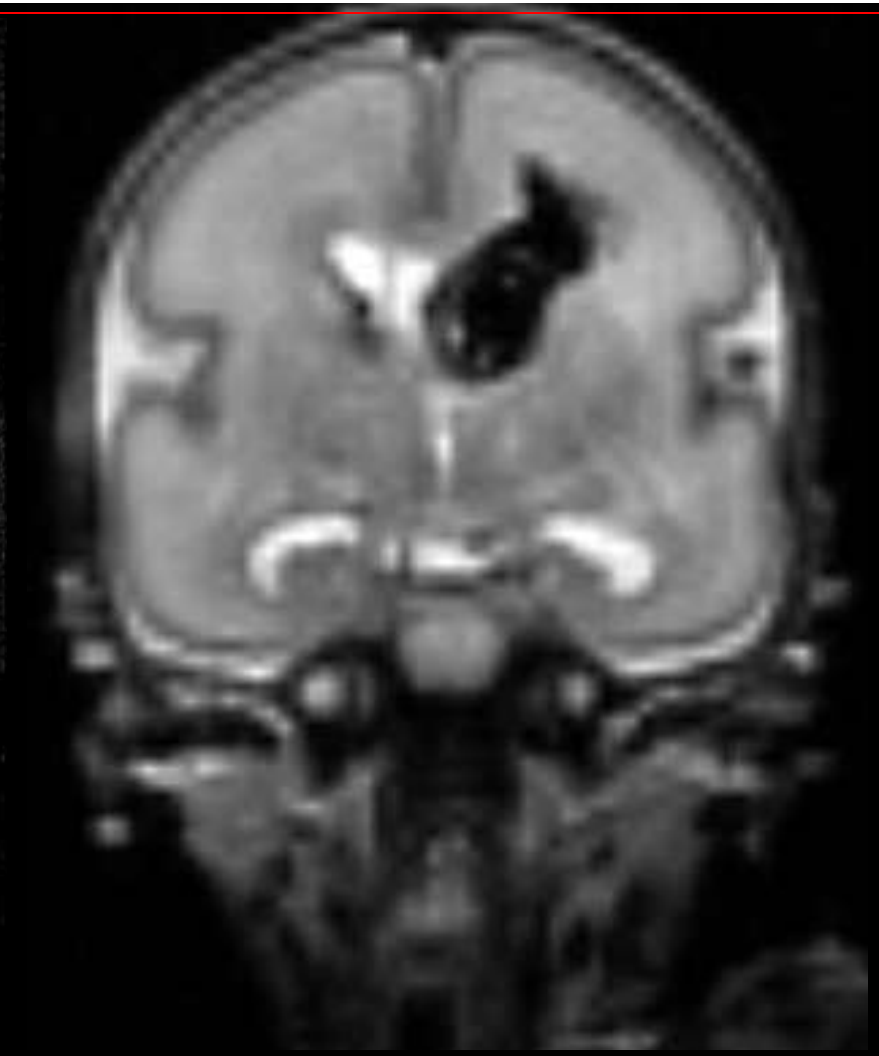
Intraventricular Hemorrhage (IVH)

Intraventricular Hemorrhage

- Includes subependymal hemorrhage (SEH), intraventricular hemorrhage (IVH) and intraparenchymal hemorrhage (IPH)
- Classification:
  - I – SEH
  - II – IVH smaller/without ventriculomegaly
  - III – IVH larger/with ventriculomegaly
  - IV – Intraparenchymal Hemorrhage

Grade IV Intraventricular Hemorrhage





Neuro-imaging and IVH

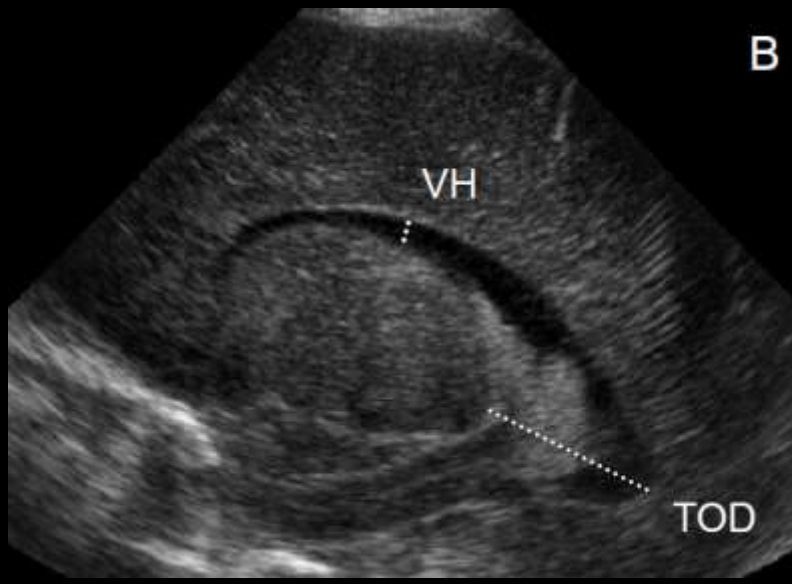
- Cranial ultrasound has good sensitivity for hemorrhage
- CUS from 326 infants had good agreement for grade III or IV IVH (>90%) but poor-to-fair for grade I/II IVH (48%-68%)
  - *Hintz et al J Peds 2007;150:592-6*
- Improved prognosis with more frequent ultrasound scans
  - *DeVries LS et al. J Peds 2004;144:815-20*

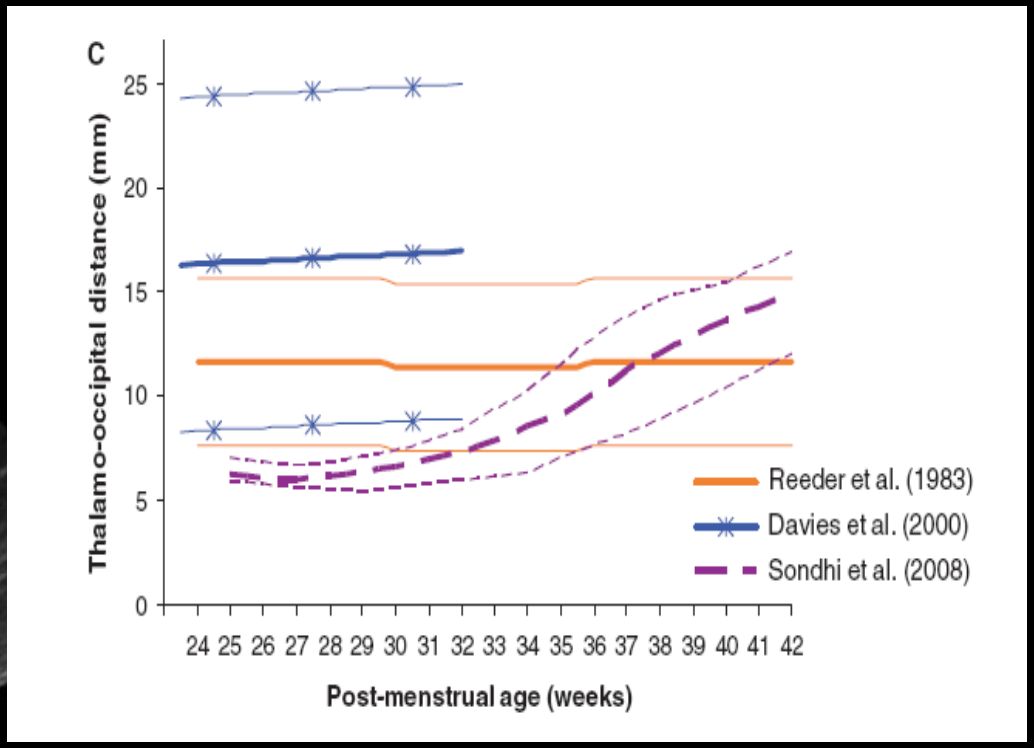
PHVD

- Accounts suggest that increase in adverse outcome from 55% to 78% in Grade 3, 63% to 92% in Grade 4 when VP shunt required
- CP Rates 7.4% (Grade 3), 48% (Grade 4)
- Early intervention (exceeding 97th) may improve outcome
  - *Brouwer et al J Pediatr 2008;152:648-54)*

Ultrasound measures

Brouwer et al Acta Pediatrica 2010 (in press)



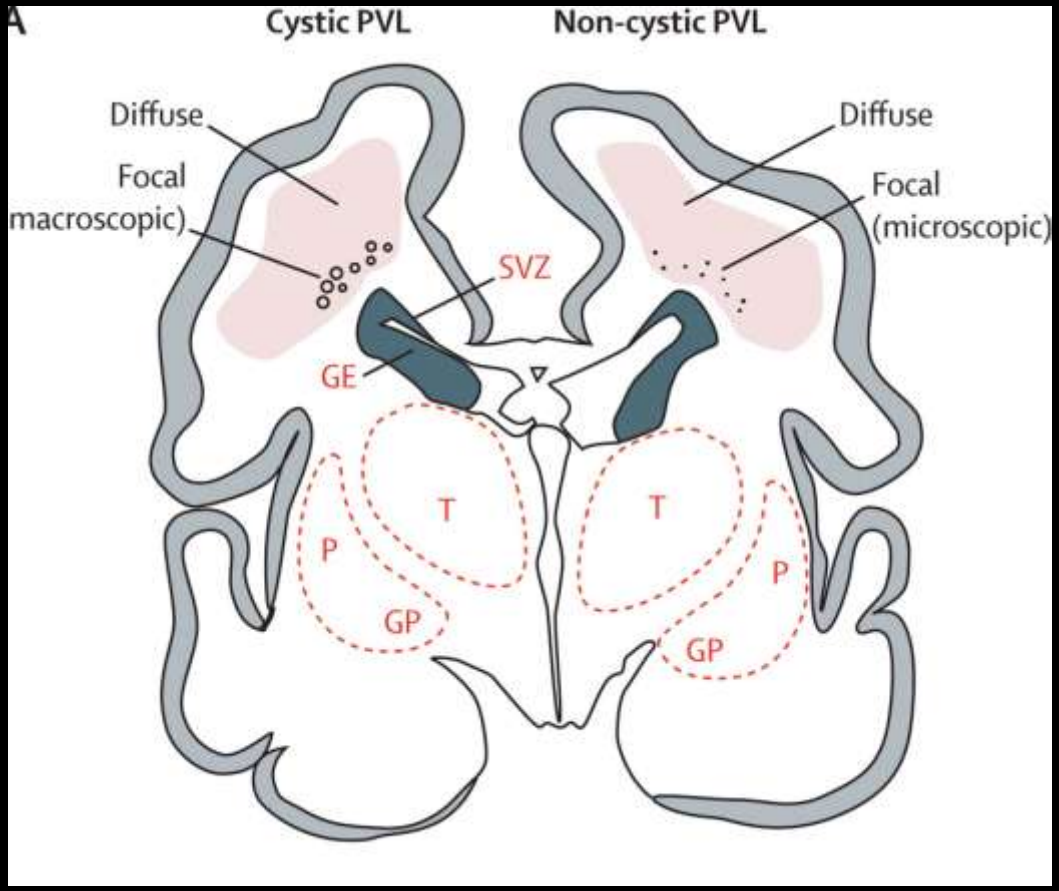


Cerebellar Hemorrhage

- Low detection on cranial ultrasound
- Estimated 20% of VLBW infants
- Major overlap mechanistically with IVH
- Current St Louis study 23% infants <30 weeks gestation with only 3/25 detected on CUS
- Outcome
  - 40% cognitive, motor and social-communication disorders
    - *Limperopoulos Pediatrics 2007;120:584-93*

Periventricular Leukomalacia (PVL)

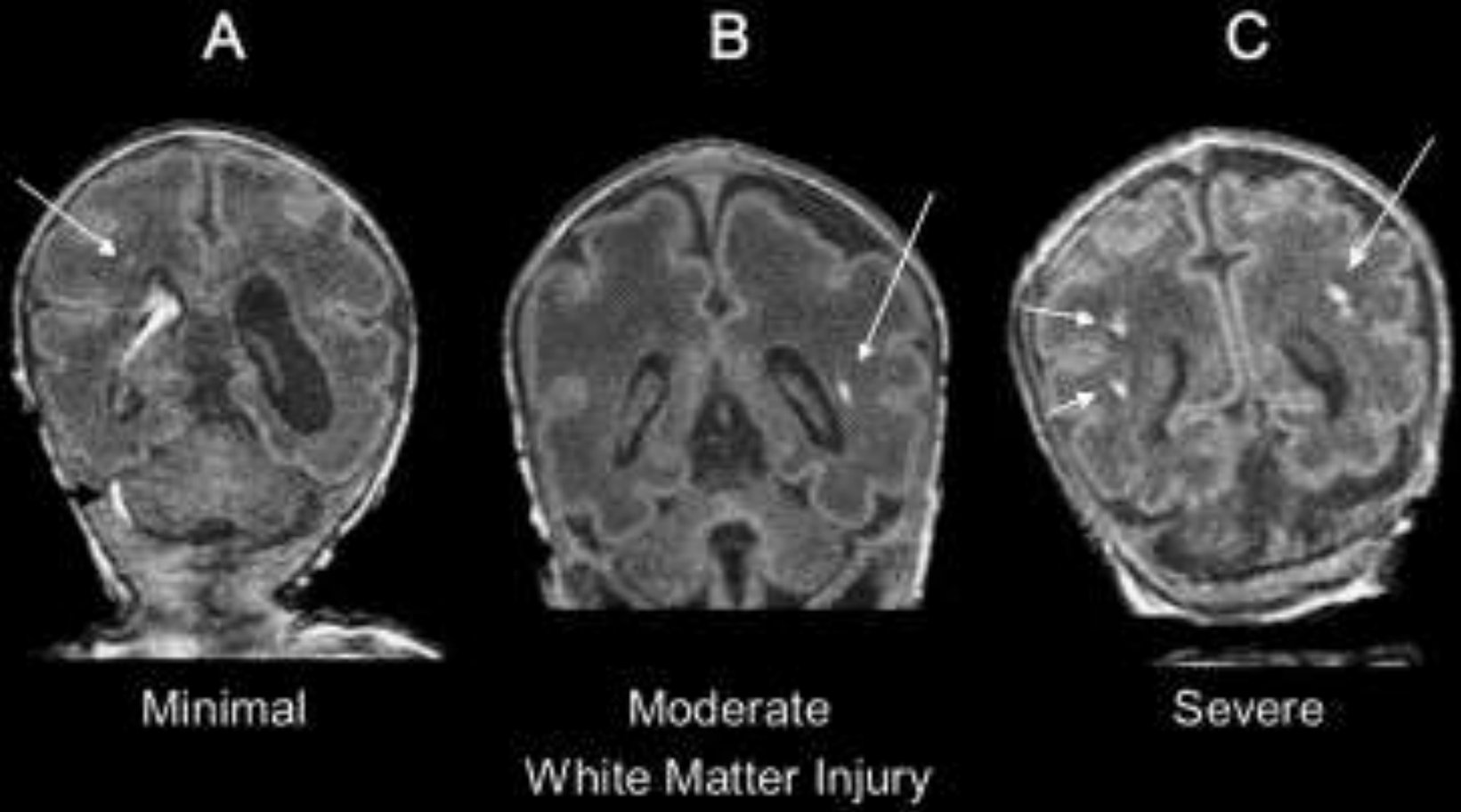
White matter Abnormalities



- Terminology
  - White matter cysts
  - White matter punctate lesions
  - Loss of white matter volume
  - Diffuse high signal changes throughout white matter

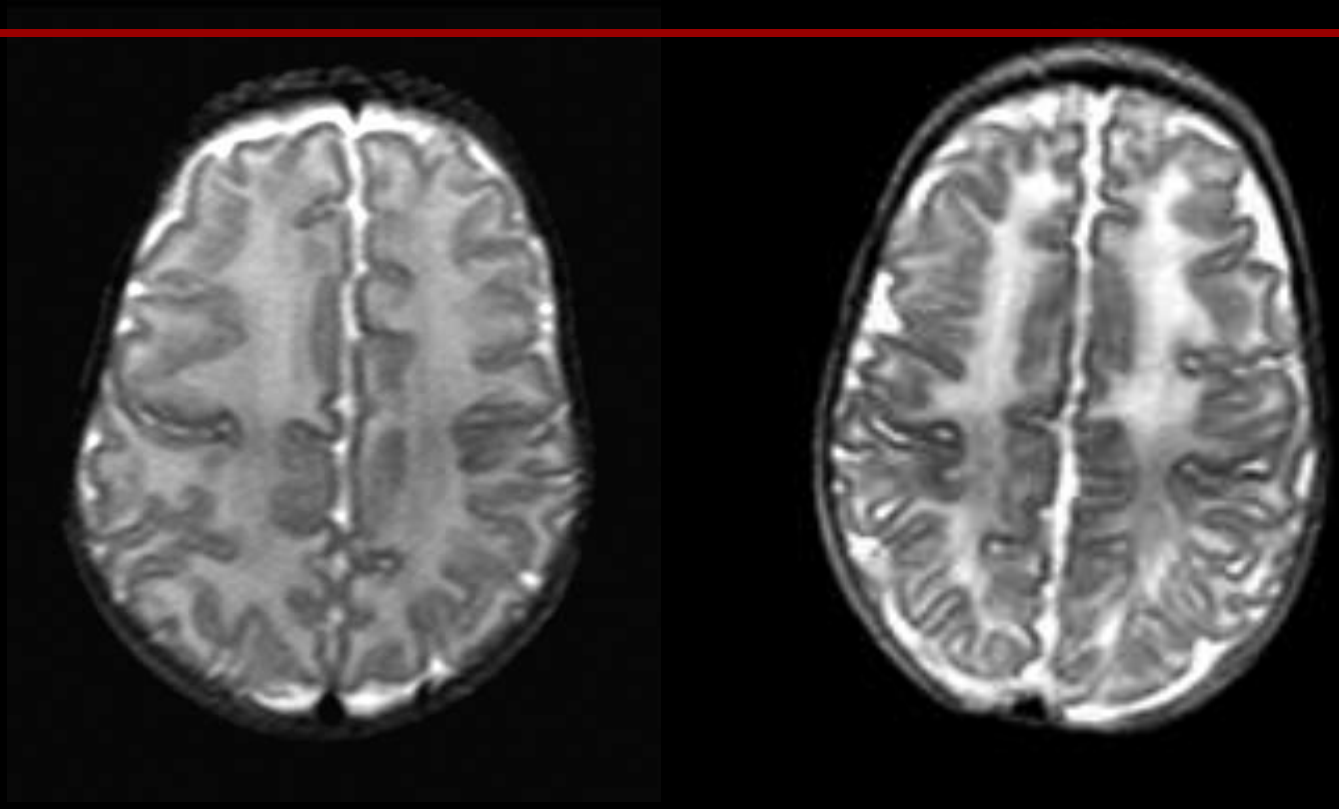
Volpe JJ Lancet Neurology 2009;8:110-24

White matter abnormalities



Miller SP et al J Pediatrics 2005;147:467-74

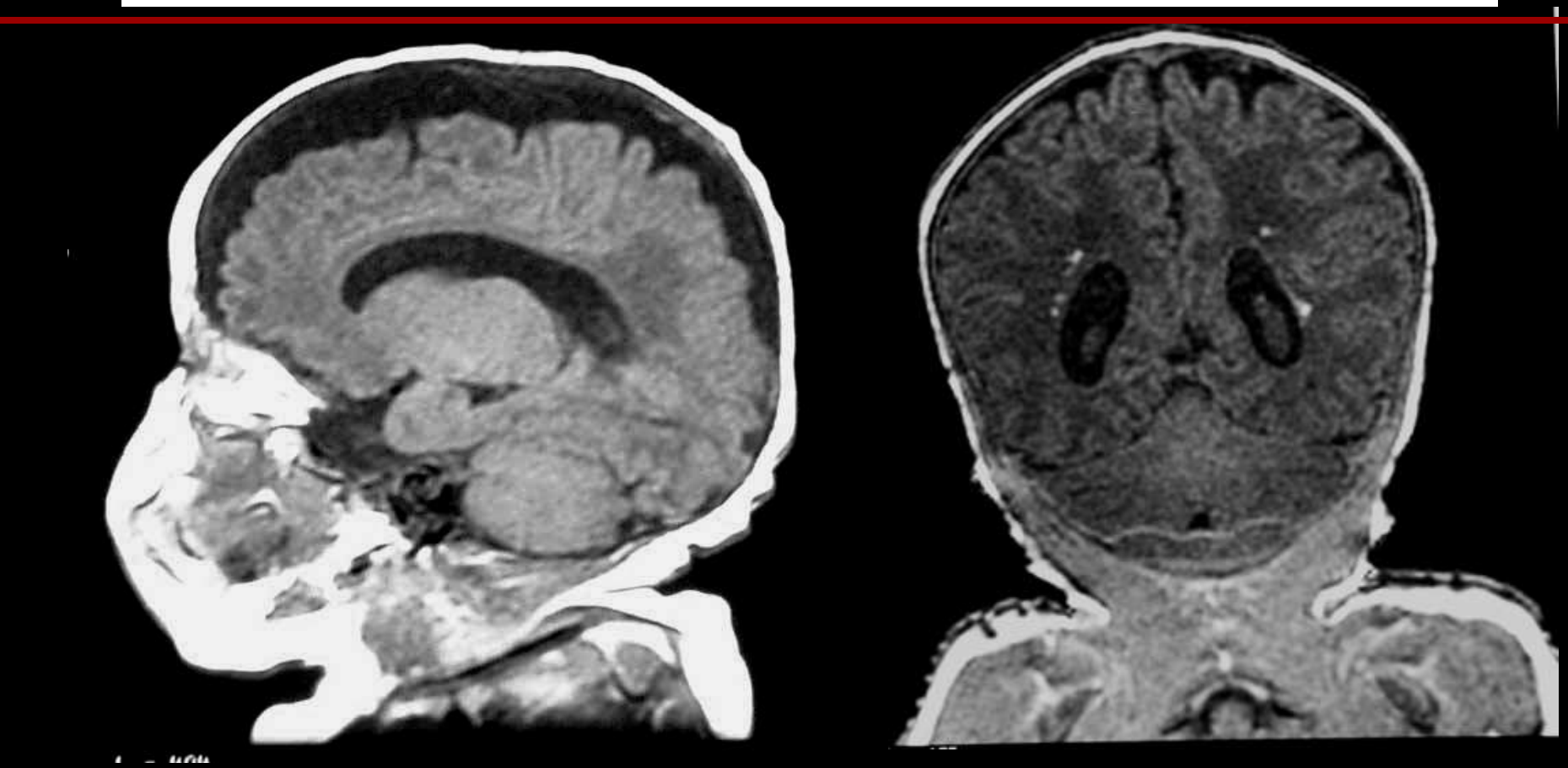
Diffuse Excessive High Signal Intensity (DEHSI)



Reported in upto 75% preterm at term

Malalouf et al Pediatrics 2001;107:719-27

White matter abnormalities



MRI WMI at Term Predicts Neurodevelopmental in the Premature Infant

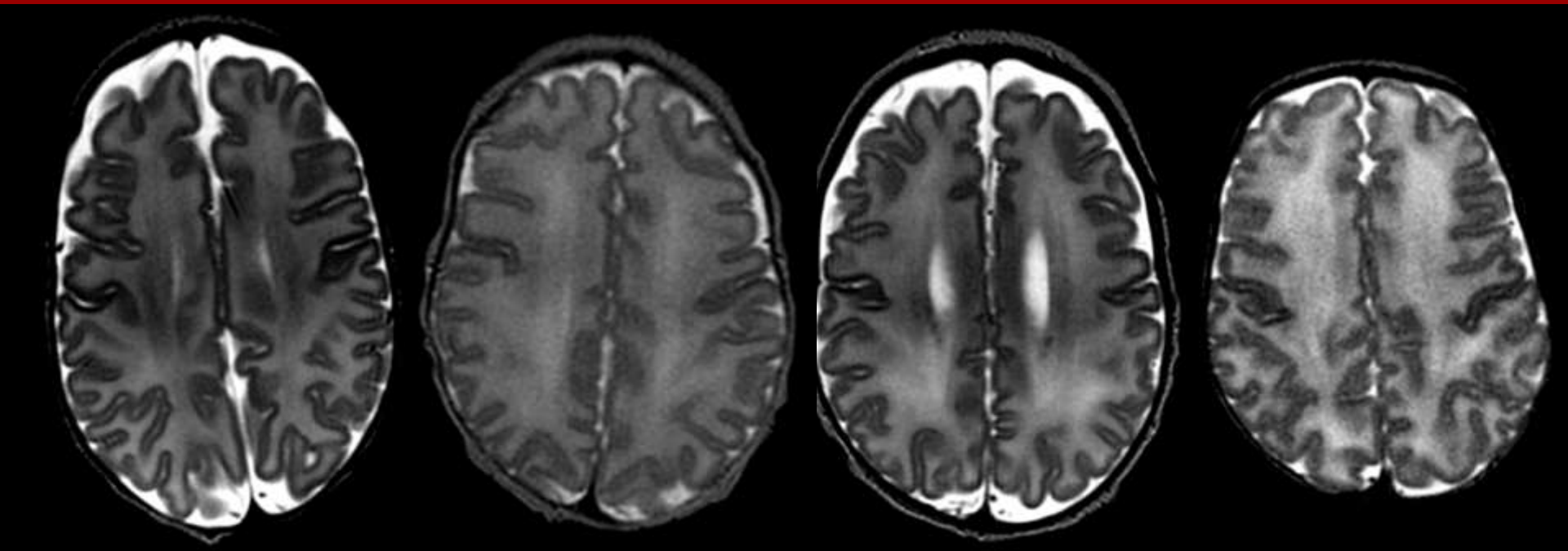
Extent of White Matter Abnormality						
Outcome	None (N=49)	Mild (N=78)	Mod. (N=26)	Severe (N=7)	F/X^2	p
M (SD) MDI score	92.5 (15.7)	85.3 (14.2)	77.6 (17.2)	69.7 (25.2)	124.8	<.0001
M (SD) PDI score	94.6 (13.6)	90.9 (11.0)	80.1 (17.5)	56.2 (25.4)	36.8	<.0001
% Cognitive delay (>2SD)	6.5	15.3	29.6	50.0	10.80	.008
% Motor delay (>2SD)	4.3	4.7	25.9	66.7	32.3	<.0001
% Cerebral palsy	2.0	6.0	24.1	66.7	25.7	<.0001

Woodward LJ et al NEJM 2006; 355(7):685-94.

Prediction of outcome - MRI scan

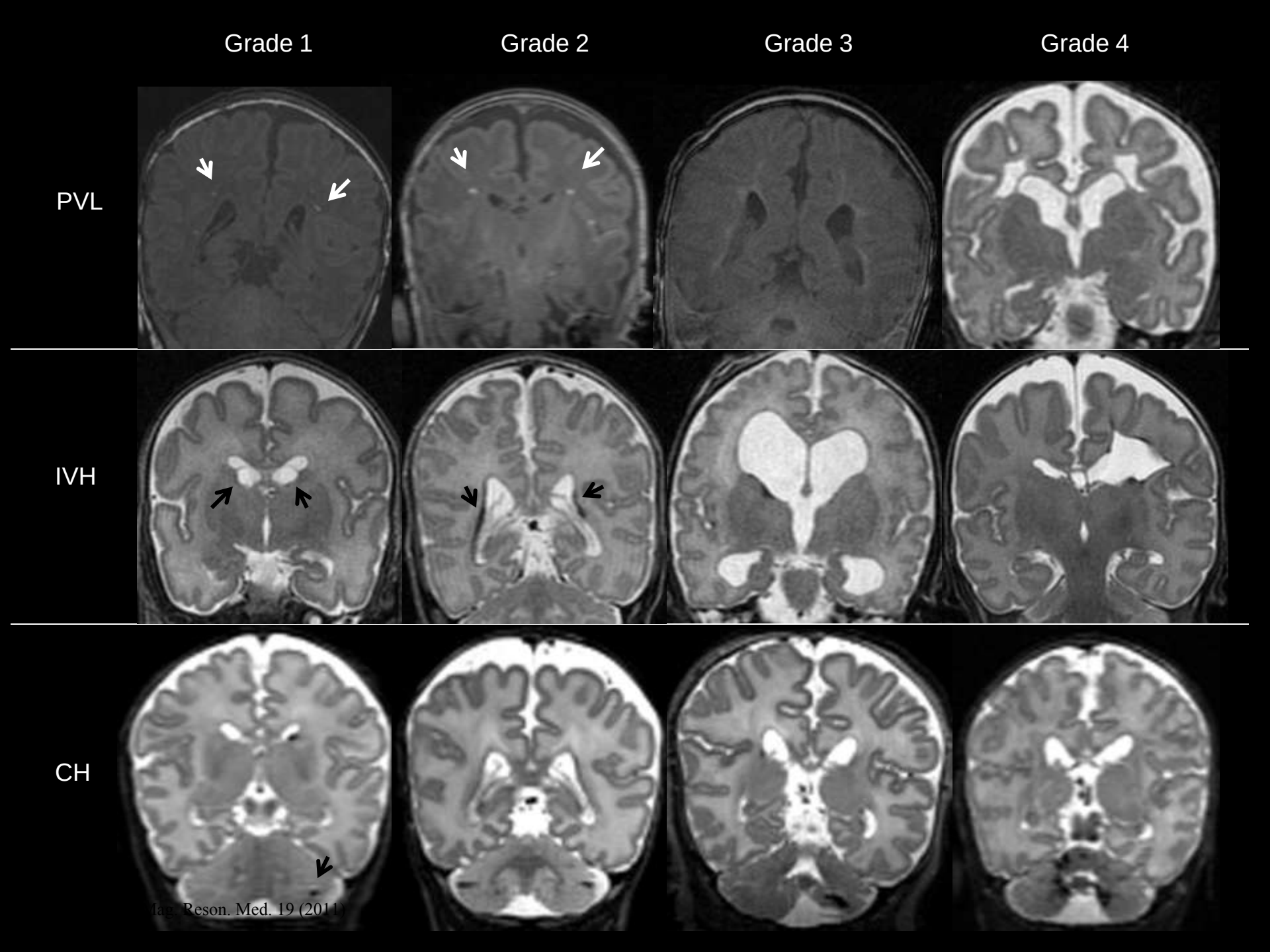
- Cerebral palsy (approximately 10%) were predicted with high sensitivity 85% and specificity 84 - 89%.
- Moderate/severe cognitive deficits (30%) were predicted with high sensitivity 89-90% and lower specificity 25-31%.
  - *Woodward et al NEJM 2006; 355(7):685-94*
  - *Dyet LE et al. Pediatrics. 2006;118(2):536-548.*
  - *Mirmiran M et al. Pediatrics. 2004;114(4):992-998.*

DEHSI (n=160)



DEHSI and Outcome

	Ⅰ N=12	Ⅱ N=35	Ⅲ N=32	Ⅳ N=50	Ⅴ N=22	P
MDI, scores(SD)	83.0(20.7)	84.1(17.1)	82.2(18.5)	90.1(18.2)	80.6(21.8)	0.24
Delayed MDI<70, n (%)	3(23.1)	5(14.3)	5(15.6)	6(11.8)	6(27.3)	0.52
PDI, scores(SD)	89.6(20.0)	87.2(19.7)	85.3(18.0)	89.9(15.2)	91.3(11.6)	0.68
Delayed PDI<70, n (%)	2(15.4)	5(14.3)	6(18.8)	5(9.8)	2(9.1)	0.77
Cerebral Palsy, n (%)	1	2	1	1	0	0.67



Diag. Reson. Med. 19 (2011)

PVL							
	Grade 4						
	Grade 3						
	Grade 2						
	Grade 1						
IVH							
	Grade 4						
	Grade 3						
	Grade 2						
	Grade 1						
CH							
	Grade 4						
	Grade 3						
	Grade 2						
	Grade 1						
No injury		220	86.4(17.9)	28(13.5)	89.4(15.3)	21(10.1)	10(4.5)

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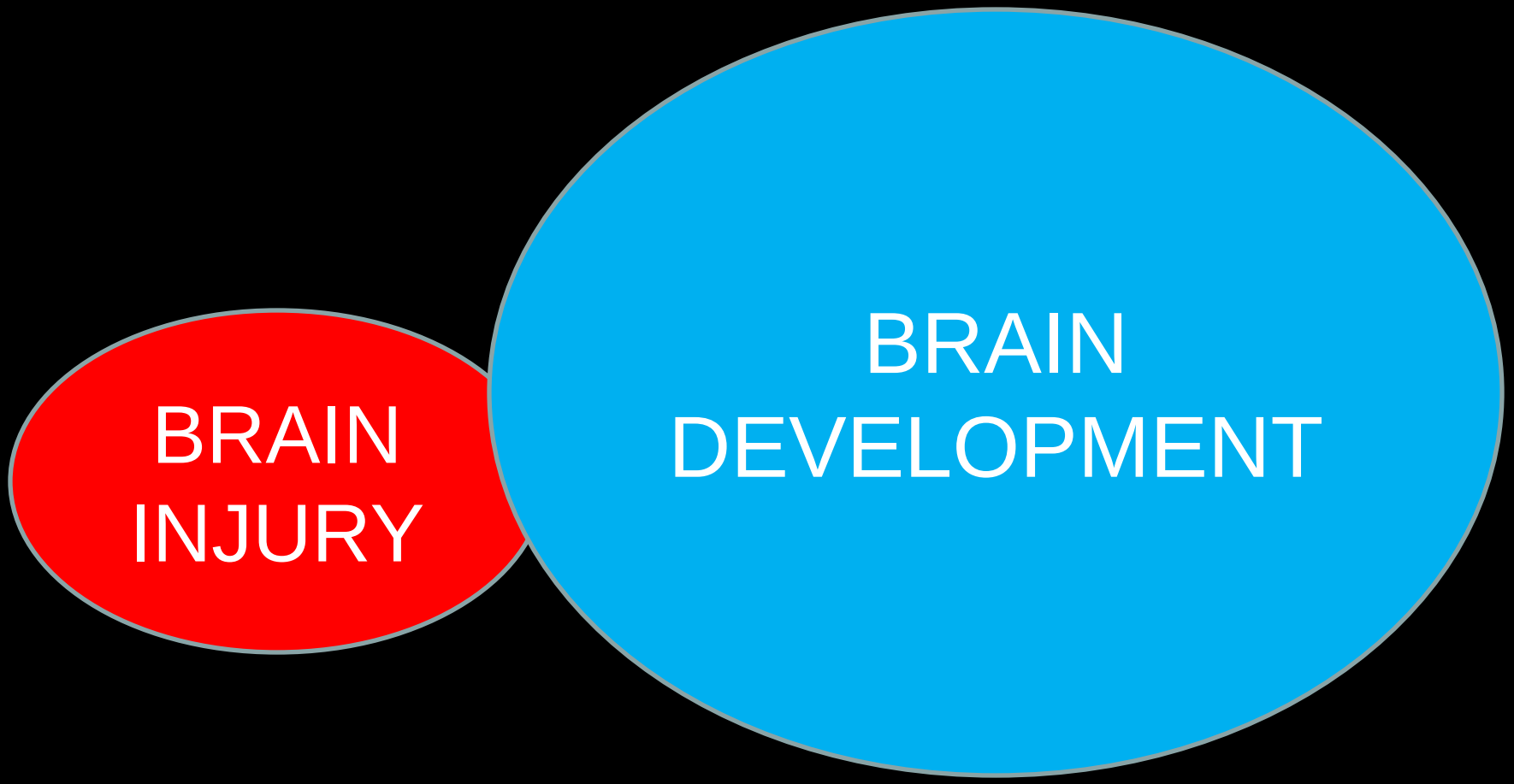
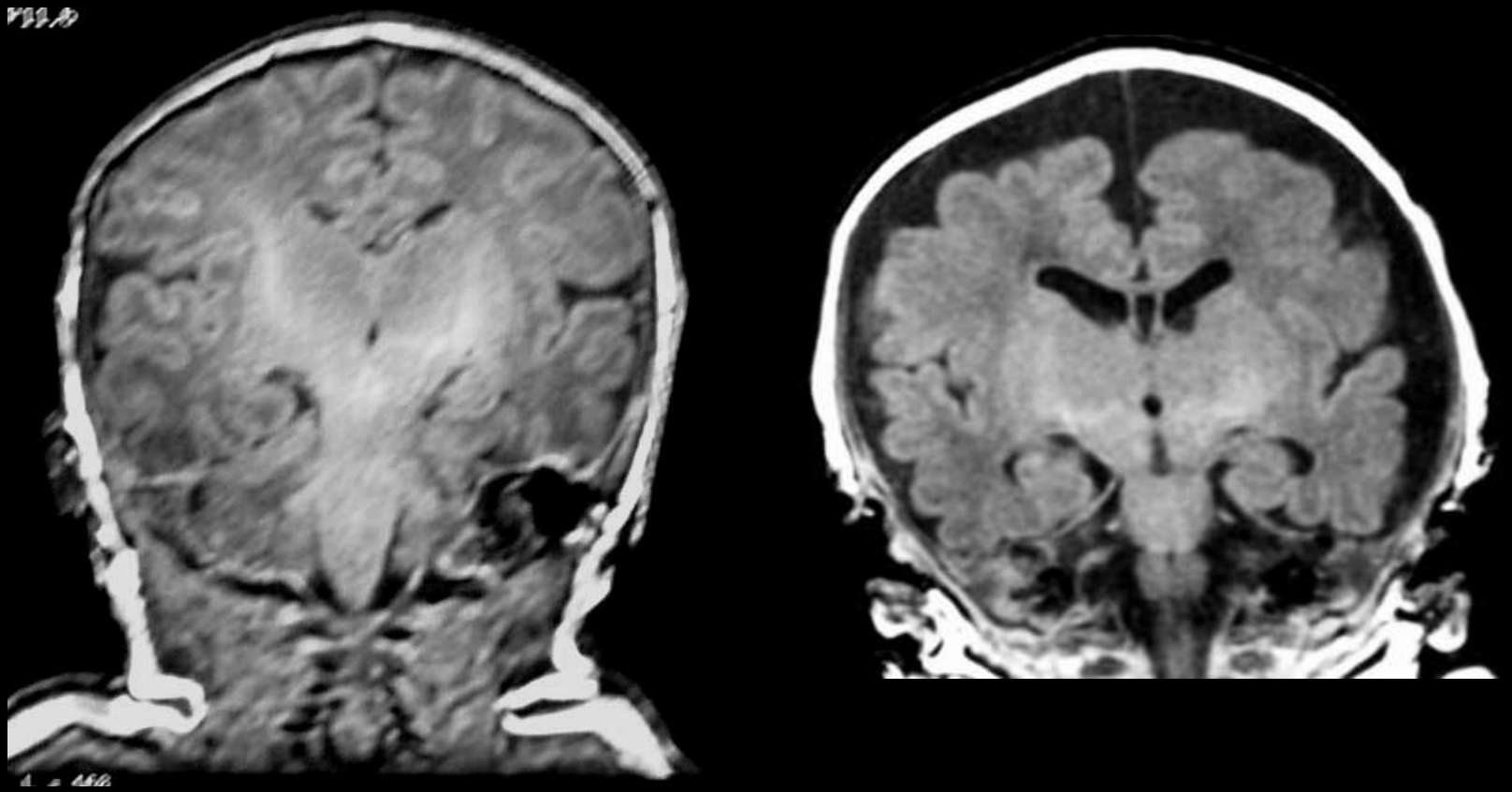
		No.	MDI Score (SD)	MDI<70 No. (%)	PDI Score (SD)	PDI<70 No. (%)	Cerebral palsy No. (%)
PVL		34					
	Grade 4	4	49.3(18.5)	3(75.0)	49.3(18.5)	3(75.0)	4(100)
	Grade 3	5	61.2(20.4)	3(60.0)	55.6(29.4)	4(80.0)	4(80.0)
	Grade 2	14[c]	82.6(13.5)	3(21.4)	85.1(11.5)	1(7.1)	3(21.4)
	Grade 1	11[d]	85.7(20.5)	2(18.2)	86.2(18.3)	1(9.1)	1(9.1)
IVH		53					
	Grade 4	13	76.1(22.6)	4(30.8)	72.3(16.2)	4(30.8)	6(46.2)
	Grade 3	2	72.5(5.0)	2(100)	75.5(12.0)	1(50.0)	1(50.0)
	Grade 2	16	85.6(15.4)	1(6.3)	89.7(11.8)	0	1(6.3)
	Grade 1	20	88.1(14.1)	3(15.0)	90.9(12.4)	2(10.0)	1(5.0)
CH		22					
	Grade 4	1[e]	84	0	84	0	0
	Grade 3	2[f]	75.5(10.6)	1(50)	77.0(1.4)	0	1(50.0)
	Grade 2	4[a]	88.8(6.7)	0	95.3(12.2)	0	1(25.0)
	Grade 1	15[b]	84.3(15.6)	4(26.7)	87.4(17.6)	3(20.0)	2(13.3)
No injury		220	86.4(17.9)	28(13.5)	89.4(15.3)	21(10.1)	10(4.5)


BRAIN
INJURY
BRAIN
DEVELOPMENT

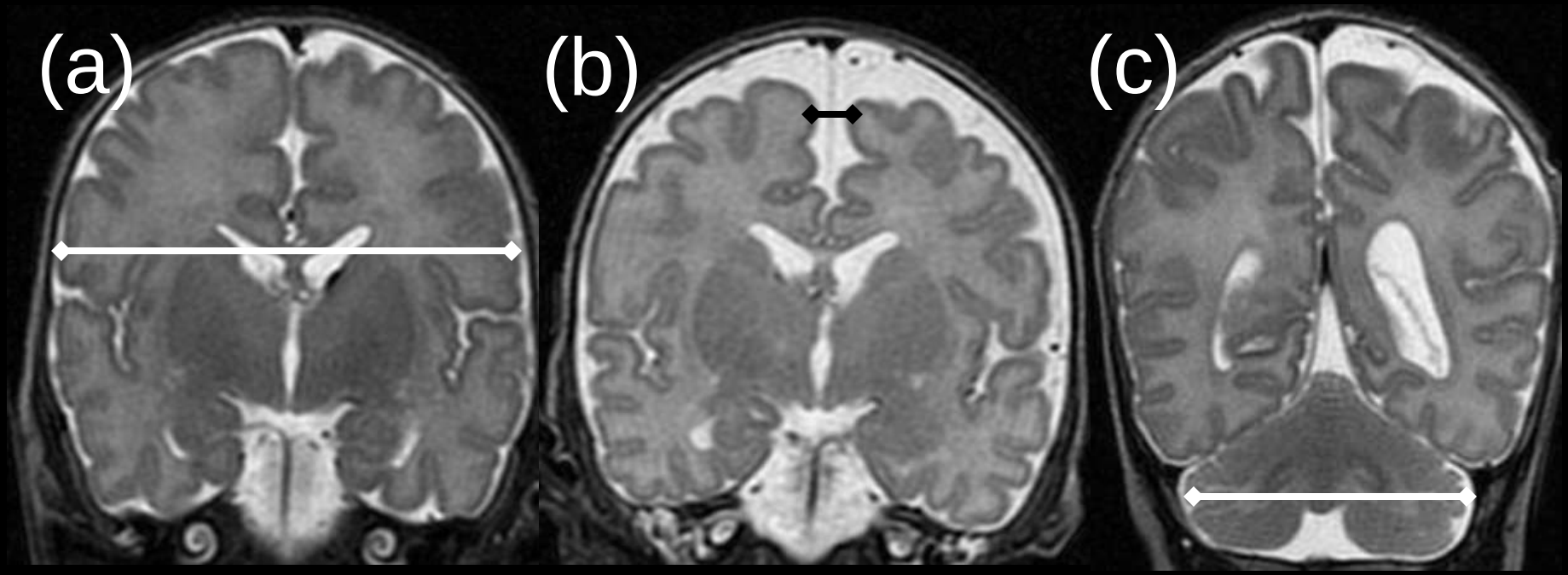
More than IVH, CH and White Matter

Diffuse Encephalopathy of Prematurity



Inder *TE et al J Peds 2003;143:171-9*

Evaluating Brain Growth at Term

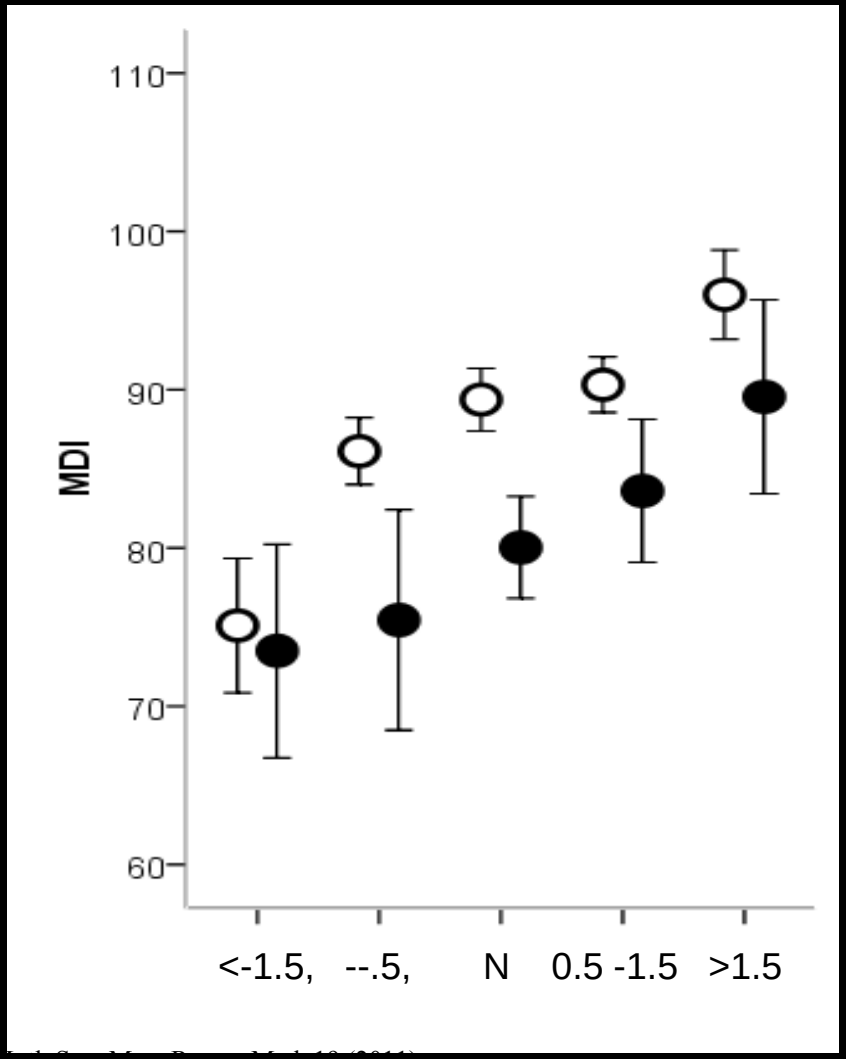


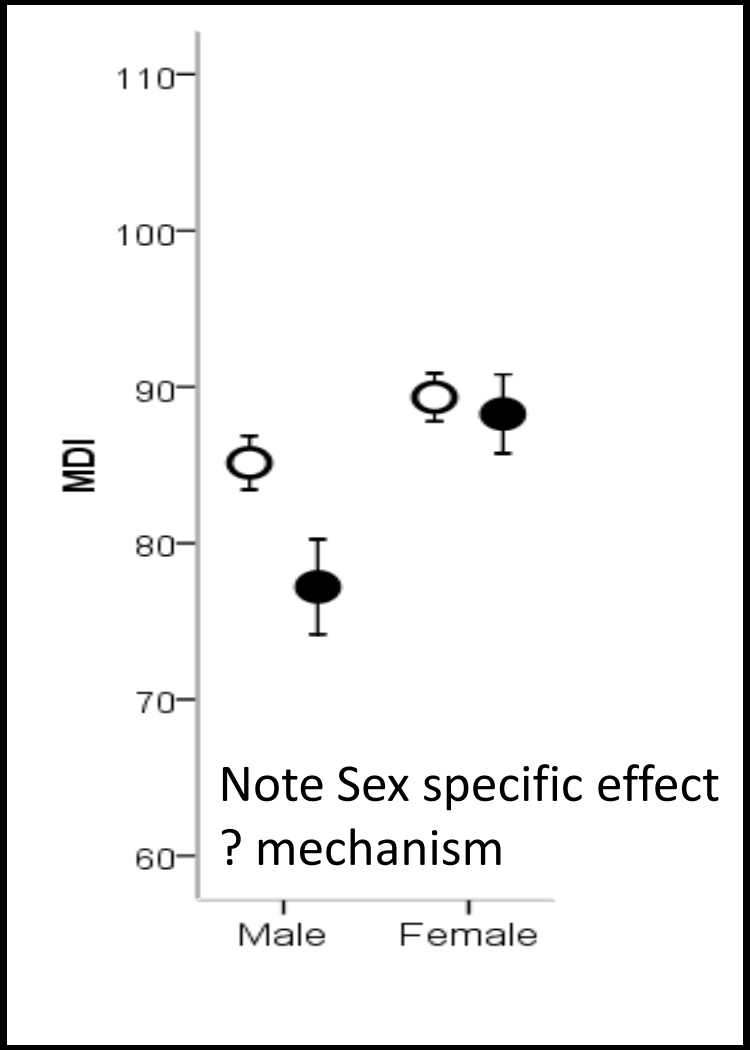
Smaller brain width relates to growth in-utero and multiple birth.
Brain width was related to cognitive outcomes at 2 years of age.

Enlarged interhemispheric space is commoner in males and influenced by dexamethasone exposure.

Fentanyl use is associated with reduction in cerebellar width

Small or hypoplastic brain





Conclusion - Neuroimaging

- Magnetic Resonance Imaging
  - All term infants with encephalopathy
  - All preterm infants <30 weeks gestation
  - At discharge or term equivalent
  - Define cerebellar hemorrhage and white matter lesions
  - Quantify cerebral growth

What does your local practice reflect?

- Magnetic Resonance Imaging
  - Do you undertake MRI scans in all term encephalopathic infants?
  - Do you undertake MRI in any preterm infants?
  - What is the quality of your MRI scans like?
  - Do you undertake any CT scans in any infants?
  - Do you use any sedation?
  - Who interprets the MRI scans?
  - Do you have a regular NICU neuroradiology session?

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