Neonatal Magnetic Resonance Imaging and Outcome at Age 30 Months in Extremely Preterm Infants

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Objective To examine associations between brain white matter abnormalities, including diffuse excessive high signal intensities, detected on neonatal magnetic resonance imaging (MRI) with neurodevelopmental outcome at age 30 months.

Study design This was a prospective, population-based study of infants born at <27 weeks gestation (n = 117) undergoing conventional MRI at term equivalent age (n = 107). At age 30 months corrected, 91 of the preterm infants (78%) and 85 term-born controls were assessed with the *Bayley Scales of Infant and Toddler Development, Third Edition* (BSID-III).

Results Cerebral palsy (CP) was present in 7% of the preterm group. On the BSID-III, mean composite scores were 96 ± 9.5 for the cognitive scale, 97 ± 14 for language scales, and 103 ± 15 for motor scales, all within the normal range for age. Compared with the term-born controls, however, the preterm infants did not perform as well on all 3 scales, also when MRI was normal. Significant associations were seen between moderate to severe white matter abnormalities and CP ($P < .001$). The presence of diffuse excessive high signal intensities was not associated with performance on the BSID-III or with CP.

Conclusion This 3-year cohort of extremely preterm infants had low rates of major brain injury and impaired outcome. Neonatal MRI provides useful information, but this information needs to be treated with caution when predicting outcome. *(J Pediatr 2012;160:559-66)*.

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Brain injury and subsequent major neuromotor difficulties are well-known consequences after very preterm birth.[1-3] As the survival of extremely preterm infants has increased over the last several decades,[4,5] many have feared a corresponding increase in long-term morbidities.[6] Although the incidence of major neuromotor impairments (ie, cerebral palsy [CP]) has remained constant[7] or even decreased,[8-10] today there is a greater awareness of the potential cognitive and behavioral problems in extremely preterm infants.[11-13]

Magnetic resonance imaging (MRI) is widely used to examine the newborn brain, both with regard to development and injury and in attempts to improve prediction of outcomes.[14] Even though classic cystic periventricular leukomalacia has become rare,[15] the incidence of noncystic white matter damage remains high.[16] Furthermore, regions with diffuse and excessive high signal in the periventricular and subcortical white matter on T2-weighted MRI (diffuse excessive high signal intensities [DEHSI][17]) are present in a large proportion of extremely preterm infants at term corrected age.[17-19] The implications of DEHSI for later outcome are unclear, however.

The aims of the present study were to investigate developmental and neurologic outcome at 30 months corrected age of a 3-year cohort of extremely preterm infants born in Stockholm, Sweden and to examine how brain white matter abnormalities detected on MRI at term equivalent age relate to outcome.

Methods

The Regional Ethics Committee in Stockholm approved the study and informed consent was obtained from all parents of the participating infants. All infants

BSID-III	*Bayley Scales of Infant and Toddler Development, Third Edition*
CP	Cerebral palsy
DEHSI	Diffuse excessive high signal intensities
FOV	Field of view
GA	Gestational age
MRI	Magnetic resonance imaging
TE	Echo time
TR	Repetition time

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Supported by the Swedish Medical Research Council (grant 2006-6151), a regional agreement for medical training and clinical research (ALF 20090177) between the Stockholm County Council and the Karolinska Institute, the Linnea and Josef Carlsson Foundation, the Swedish Order of Freemasons, the Swedish Medical Society, the Jerring Foundation, and Sällskapet Barnavård. B.V. was supported by a Marie Curie Individual Intra-European Fellowship within the EU FP6 Framework Program. The authors declare no conflicts of interest.

 10.1016/j.jpeds.2011.09.053

born in Stockholm with a gestational age (GA) of <27 weeks 0 days were included in the study. During the 3-year study period from January 1, 2004, to March 31, 2007, 192 infants were born alive and 129 (69%) survived to term age (mean GA, 25 weeks 4 days ± 1 day; mean birth weight, 808 ± 160 g). Children with malformations, chromosome aberrations, and congenital infections were excluded. Eight infants met the exclusion criteria, 4 families moved from the region, 9 declined participation in the MRI examination, and 1 infant was too unstable for MRI scanning (**Figure 1**; available at www.jpeds.com). Thus, 107 extremely preterm infants underwent MRI at term equivalent age (38-41 weeks GA). A control group of 85 term-born control infants with similar age and sex distribution underwent the same follow-up assessments but did not undergo neonatal MRI.

All imaging was performed on a Philips Intera 1.5-T MRI system (Philips, International, Amserdam, The Netherlands). Early in the study period, infants were given a low dose of chloral hydrate (30 mg/kg) orally or rectally before the examination. During the last year of the study, most infants were scanned during natural sleep.

MRI data were acquired using a 6-channel receive-only head coil. The MRI protocol consisted of sagittal T1-weighted turbo spin-echo images (echo time [TE], 9 ms; repetition time [TR], 600 ms; flip angle, 90 degrees; voxel size, 0.7 × 0.7 × 4 mm; echo train length, 3; field of view [FOV], 180 mm), sagittal T2-weighted turbo spin echo images (TE, 100 ms; TR, 5000 ms; flip angle, 90 degrees; voxel size, 0.7 × 0.7 × 3 mm; echo train length, 16; FOV, 180 mm), axial T2*-weighted turbo spin-echo images (TE, 100 ms; TR, 5000 ms; flip angle, 90 degrees; voxel size, 0.7 × 0.7 × 4 mm; echo train length, 16; FOV, 180 mm), axial T2*-weighted fast field echo images (TE, 23 ms; TR, 586 ms; flip angle, 18 degrees; voxel size, 2.8 × 2.8 × 4.5 mm; FOV, 180), axial inversion recovery images (TE, 15 ms; TR, 3500 ms; flip angle, 90 degrees; voxel size, 0.9 × 0.9 × 4 mm; inversion recovery, 400 ms; FOV, 180 mm) and a 3-dimensional T1-weighted gradient echo image (TE, 4.6 ms; TR, 40 ms; flip angle, 30 degrees; voxel size, 0.7 × 0.7 × 0.1 mm; FOV, 180 mm).

Images were evaluated by 4 independent observers using a scoring system for white matter abnormalities,[20] judging 5 separate items: abnormal white matter signal, reduced white matter volume, cystic changes, myelination/thinning of the corpus callosum, and ventricular dilatation. Based on the composite score calculated from the individual items, MRI images were assigned to 4 groups: no, mild, moderate, or severe white matter abnormalities (**Figure 2**). Because of the low number of infants with moderate to severe white matter abnormalities, the 4 groups were pooled into 2 categories, no-mild and moderate-severe white matter abnormalities. In addition, DEHSI in the periventricular white matter were identified (**Figure 2**). The interobserver agreement was 98%, and consensus was reached after discussion when opinions differed on first assessment.

At age 30 months corrected, each infant was assessed with the *Bayley Scales of Infant and Toddler Development, Third*

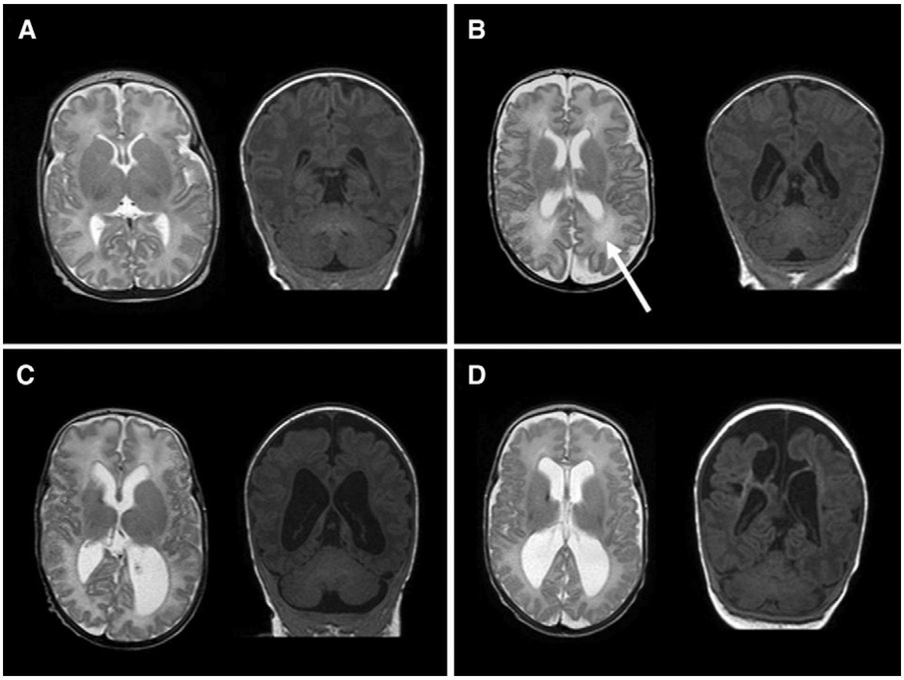

Figure 2. Scoring of white matter abnormalities on conventional MRI (axial T2-weighted and coronal T1-weighted images): **A**, normal white matter; **B**, mild abnormalities; **C**, moderate abnormalities; **D**, severe abnormalities. DEHSI are indicated with an *arrow*.