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Late Gestation Cerebellar Growth Is Rapid and Impeded by Premature Birth

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ABSTRACT. *Objective.* **Cognitive impairments and academic failure are commonly reported in survivors of preterm birth. Recent studies suggest an important role for the cerebellum in the development of cognitive and social functions. The objective of this study was to examine the impact of prematurity itself, as well as prematurity-related brain injuries, on early postnatal cerebellar growth with quantitative MRI.**

Methods. **Advanced 3-dimensional volumetric MRI was performed and cerebellar volumes were obtained by manual outlining in preterm (<37 weeks) and healthy term-born infants. Intracranial and total brain volumes were also calculated.**

Results. **A total of 169 preterm and 20 healthy full-term infants were studied; 145 had preterm MRI (pMRI), 75 had term MRI (tMRI), and 51 underwent both pMRI and tMRI. From 28 weeks' postconceptional age to term, mean cerebellar volume (177%) in preterm infants increased at a much faster rate than did mean intracranial (110%) or mean brain (107%) volumes. Smaller cerebellar volume was significantly related to lower gestational age at birth and to intracranial and total brain volumes. Mean cerebellar volume of preterm infants at tMRI was significantly smaller than the volumes of term-born infants. Cerebellar growth impairment was correlated strongly with associated brain injuries, even in the absence of direct cerebellar injury.**

Conclusions. **Our data suggest that the growth of the immature cerebellum is particularly rapid during late gestation. However, this accelerated growth seems to be impeded by premature birth and associated brain injury. The long-term neurodevelopmental disabilities seen in survivors of premature birth may be attributable in part to impaired cerebellar development.** *Pediatrics* **2005;115: 688–695;** ***premature infants, magnetic resonance, cerebellum, brain injury, development.***

ABBREVIATIONS. PT, preterm; TB, term born; PDA, patent ductus arteriosis; pMRI, preterm MRI; tMRI, term MRI; 3D, 3-dimensional; SPGR, spoiled gradient recalled; CSF, cerebrospinal fluid; IVH, intraventricular hemorrhage.

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Brain injury in the premature infant is a problem of great magnitude, with potential lifelong disability of the infant and enormous impact on the family and society. Survivors of preterm (PT) birth are at increased risk for cerebral palsy, and up to half of survivors exhibit later cognitive, learning, and behavioral difficulties.[1–3] To date, clinical and research activity has focused largely on supratentorial injuries such as periventricular leukomalacia and intraventricular hemorrhage.[4–8] Conversely, injury to the cerebellum in the premature infant has been relatively underrecognized before the advent of more sophisticated neuroimaging techniques.[9] Furthermore, our understanding of the relationship among PT birth, brain injury, and subsequent cerebellar development, both structural and functional, remains limited.

Survivors of PT birth exhibit a constellation of motor deficits, including impaired fine motor function, coordination, and motor sequencing,[10–12] deficits traditionally ascribed to cerebellar injury. Moreover, recent studies support an important role for the cerebellum in nonmotor functions such as cognition, language, and social function.[13,14] Reports in older children with a history of PT birth[2,15] have shown smaller cerebellar volumes compared with those of term-born (TB) children. Recently, Allin et al[15] proposed a causative relationship between impaired cerebellar growth and cognitive deficits in premature infants.

Quantitative MRI studies in PT infants have demonstrated dramatic increases in brain growth (and its tissue subclasses) and microstructural organization of the brain after premature birth.[16–18] It has been proposed that this rapid growth phase may render the brain particularly vulnerable to injury and to subsequent impaired growth of cerebral cortical gray matter and myelinated white matter, as well as disturbed development of white matter microstructure.[7] However, to date, the early time course of cerebellar growth in premature infants has not been examined; hence, the onset of cerebellar growth failure in these infants remains unknown. Because cerebellar injury is now increasingly recognized in PT infants, the impact of such injury on subsequent cerebellar development is important to address. Therefore, the primary objective of this study was to define the rate of cerebellar growth in the PT infant and the impact

of prematurity itself, as well as prematurity-related brain injuries, on this growth.

METHODS

Selection Criteria

Our quantitative MRI measurements were made on existing MRI data sets from previous and ongoing prospective research studies of PT infants (≤37 weeks' gestational age) and healthy TB infants (>37 weeks gestational age).[16] We did not use MRI scans that were performed for clinical diagnostic purposes. All studies were performed with informed parental consent and in accordance with the ethical standards of the Institutional Review Board, Brigham and Women's Hospital. We excluded MRI scans from infants with known or suspected brain malformation; dysmorphic features; or congenital anomalies suggestive of a genetic syndrome, metabolic disorder, or central nervous system infection. In addition, we excluded scans in which the MRI data were either insufficient or of suboptimal quality for our cerebellar volumetric measurements.

Perinatal data, including birth weight, gestational age, Apgar score, gender, singleton versus multiple birth, length of intubation, need for high-frequency ventilation, presence of a patent ductus arteriosus (PDA), and length of hospitalization were collected from the infant's medical records. Infant growth parameters (eg, weight and head circumference measures) were also obtained from review of medical records made at the time of preterm (pMRI) and term MRI (tMRI) scans.

MRI Scan Acquisition

MRI scanning was performed with a 1.5-T General Electric Signa System (GE Medical Systems, Milwaukee, WI). MRI data were acquired using 2 different imaging modes: a coronal 3-dimensional (3D) Fourier transform spoiled gradient recalled (SPGR) sequence (1.5-mm slice thickness; flip angle: 45°; repetition time: 35 msec; echo time: 5 ms; field of view: 18 cm; matrix: 256 × 256) and an axial or coronal double-echo (proton density and T2-weighted) spin-echo sequence (3-mm slice thickness; repetition time: 3000 msec; echo times: 36 and 162 msec; field of view: 18 cm; matrix: 256 × 256, interleaved acquisition). The voxel dimensions for the SPGR acquisition were $0.7 \times 0.7 \times 1.5$ mm^3.

MRI Processing

Postacquisition processing was performed on workstations (Sun Microsystems, Mountain View, CA). The coronal SPGR and dual-echo sequences were registered together to form a 3-channel 3D MRI data set. Manual segmentation of the 3D data then was performed by a series of algorithms, including manual tissue classification and application of a mask to obtain volumes of cortical and subcortical gray matter, unmyelinated and myelinated white matter, and cerebrospinal fluid (CSF).[17] Cerebellar volume was measured by manual outlining on the SPGR sequence of the registered 3D MRI data using Slicer (www.slicer.org; Fig 1). The volume of the cerebellum was determined by counting the number of voxels in the segmentation and multiplying by the volume of each voxel. A single investigator (C.L.) performed all manual outlining of the cerebellum, with an intrarater reliability coefficient (10 MRI scans) of $\alpha = .96$.

Intracranial cavity volume was determined from the sum of the voxels representing all gray and white matter voxels of the brain (including cerebrum, cerebellum, and brainstem) plus the CSF voxels. Total brain volume was calculated from the sum of the voxels representing all gray and white matter voxels of the brain but without the CSF voxels.

MRI Abnormalities

Intracranial lesions were categorized by conventional T1/T2-weighted MRI as supratentorial lesions, infratentorial lesions, or combined supratentorial and infratentorial lesions. Supratentorial lesions included (1) uncomplicated intraventricular hemorrhage (IVH; germinal matrix hemorrhage, grade I and grade II IVH)[19]; (2) ventriculomegaly (secondary to atrophy, grade III IVH, or posthemorrhagic hydrocephalus); (3) parenchymal lesions, consisting of periventricular leukomalacia (including both cystic and diffuse noncystic white matter injury, the latter being characterized by diffuse and excessive high signal intensity in the periventricular white matter on T2-weighted images); and (4) periventricular hemorrhagic infarction (a unilateral or asymmetric lesion of increased T2 signal in the periventricular white matter associated with ipsilateral germinal matrix-IVH). Infratentorial lesions consisted of hemorrhagic intraparenchymal cerebellar or extraparenchymal lesions. Combined lesions were diagnosed when both supratentorial parenchymal injury and infratentorial parenchymal injury were present.

For preterm infants (≤37 weeks' postconceptional age), we compared cerebellar volumes of PT infants with normal pMRI studies with volumes of those with abnormal pMRI studies. We then compared cerebellar volumes of PT infants studied at term with the volumes of healthy TB infants. For the tMRI scans, we first compared cerebellar volumes of PT infants with normal and abnormal findings at tMRI with the volumes of TB infants. Finally, we compared the term cerebellar volumes of PT infants with abnormal conventional MRI (based on the diagnostic categories described above) with the volumes of the TB infants.

Statistical Analysis

Continuous perinatal factors were summarized using means and SDs or medians and ranges; categorical factors were summarized using proportions. Differences in perinatal characteristics for PT infants versus full-term control infants and differences in preterm measurements for PT infants with normal versus abnormal MRI were evaluated using the 2-sample *t* test, Wilcoxon rank sum test, or Fisher exact test. Comparisons of measurements at tMRI across the 3 subgroups PT with normal MRI, PT with abnormal MRI, and term controls were performed using 1-way analysis of variance or Fisher exact test. The Pearson correlation coefficient was used to measure the strength of the relationships between cerebellar volume at MRI and patient characteristics. Additional univariate and multivariate analyses were performed using linear regression analysis.

RESULTS

Patient Characteristics

We analyzed the MRI data from 169 PT infants and 20 healthy TB infants. Table 1 summarizes the perinatal characteristics of these PT and TB infants. Of the PT infants studied, 94 had an MRI study before or at 37 weeks' postconceptional age (ie, pMRI) at a mean of 32.8 weeks (±2.6 weeks), 24 had a tMRI scan at approximately term postconceptional age (mean: 40.1 ± 1.5 weeks), and 51 had both pMRI and tMRI

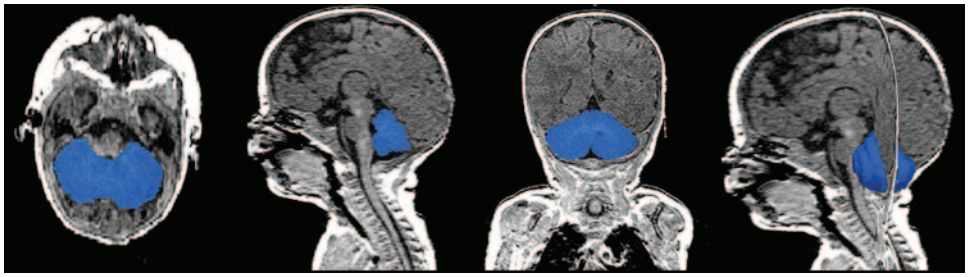

Fig 1. Manual cerebellar outlining of reconstructed 3D image slices using 3D Slicer software.

TABLE 1. Perinatal Characteristics of the PT and TB Infants

Parameter	Preterm Infants (n = 169)	Full-Term Controls (n = 20)
Gestational age, wk, mean ± SD (range)	29.1 ± 3.4 (23–37)	39.6 ± 0.8 (38–41)
Birth weight, g, mean ± SD (range)	1341 ± 553 (505–3033)	3625 ± 497 (2835–4742)
Male, n (%)	89 (53%)	10 (50%)
Singleton, n (%)	90 (54%)	20 (100%)
Apgar (1 min), mean ± SD (range)	7 (1–9)	8 (7–9)
Apgar (5 min), mean ± SD (range)	8 (3–9)	9 (8–9)

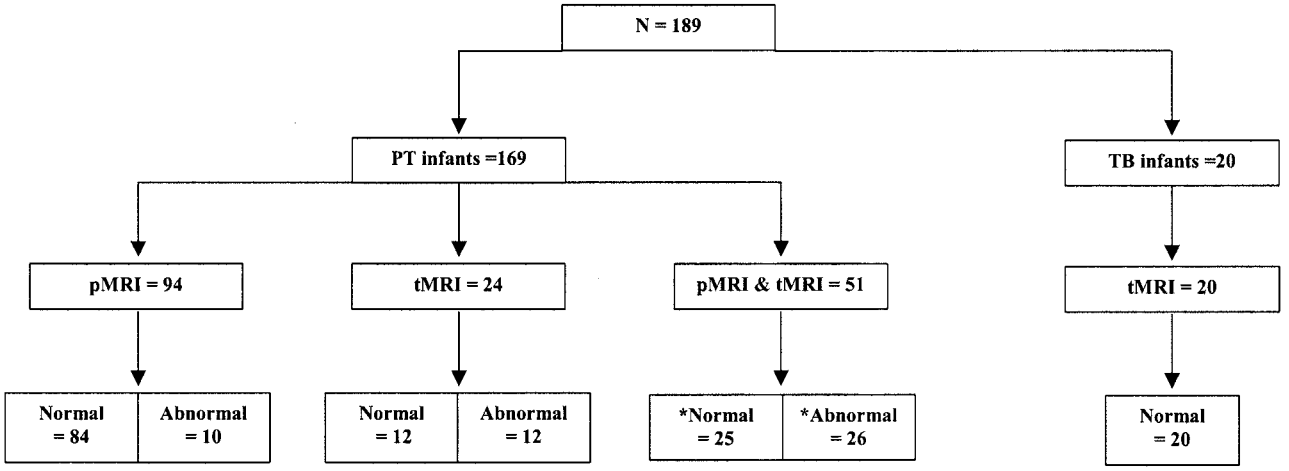

Fig 2. MRI studies in preterm and term-born infants. *For all preterm infants who had both pMRI and tMRI, scan results showed agreement (25 normal on both occasions, 26 abnormal on both occasions).

(Fig 2). Cerebellar volumes were calculated for all MRI studies (ie, at the time of pMRI scan, tMRI scan, or both) for all 189 infants, whereas intracranial cavity and total brain volumes could be determined for 141 and 97 PT infants, respectively. There were no differences in postconceptional age at pMRI between PT infants with normal and abnormal findings on conventional T1/T2 MRI scans (median postconceptional age of PT with normal MRI: 32.7 ± 2.7 weeks versus 33.1 ± 2.1 weeks for PT infants with abnormal MRI).

Conventional MRI Findings

T1/T2 MRI scans were read by an experienced pediatric neuroradiologist (R.R.) who was blinded to the clinical data. Figure 2 summarizes the distribution of all MRI studies. Among the 145 pMRIs, 109 (75%) were normal and 36 (25%) were abnormal. All PT infants with pMRI and tMRI abnormalities were ≤32 weeks' gestational age at birth. For each of the 51 PT infants with both pMRI and tMRI, there was agreement between the 2 scans (25 had normal T1/T2 studies on both occasions, whereas 26 demonstrated pMRI abnormalities that persisted at tMRI). Of the 75 PT infants with tMRI scans, 38 (51%) were abnormal. All TB infants had normal MRI scans. Table 2 summarizes the MRI abnormalities in the PT infants.

Cerebellar and Supratentorial Growth in PT Infants

Cerebellar volume increased on average by 1.57 mL (r = 0.95, $P < .001$) for each 1-week increase in postconceptional age in PT infants with normal MRI studies at pMRI and tMRI (Fig 3). Cerebellar volume at both pMRI and tMRI was significantly associated with gestational age (r = 0.89, $P < .001$) and weight at the time of the MRI (r = 0.86, $P < .0001$).

When the rate of cerebellar growth in PT infants

TABLE 2. MRI Abnormalities in PT Infants at pMRI and tMRI Studies

MRI Findings	Total Patients (n = 169)	pMRI Only (n = 94)	tMRI Only (n = 44)	Both pMRI and tMRI (n = 51)
Uncomplicated IVH	3	3	0	0
Ventriculomegaly	8	5	0	3
Supratentorial parenchymal Lesions	30	2	10	18
PVL/PVHI	20/10	1/1	7/3	12/6
Cystic PVL/noncystic PVL	4/16	1/0	0/7	2/10
Cerebellar hemorrhage (intraparenchymal)	5	2	1	2
Combined supratentorial and infratentorial lesions*	5	1	1	3

PVL indicates periventricular leukomalacia; PVHI, periventricular hemorrhagic infarction.
* Noncystic PVL and intraparenchymal cerebellar (n = 2); PVHI and intraparenchymal cerebellar (n = 1); PVHI and intraparenchymal and extraaxial cerebellar (n = 2).

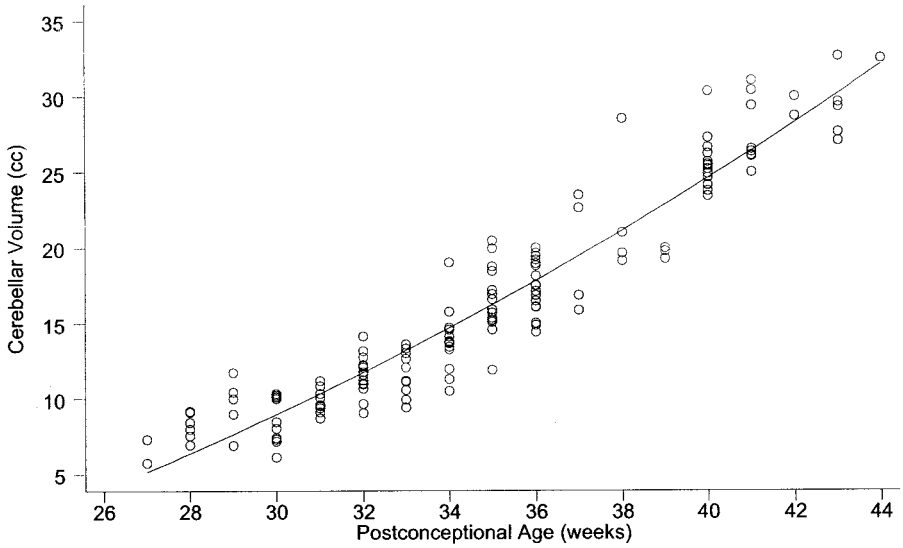

Fig 3. Relationship between cerebellar volume and postconceptional age in preterm infants with normal pMRI and tMRI.

with normal pMRI between 28 and 40 weeks' postconceptional age was compared with the rate of increase of intracranial cavity volume and total brain volume, mean cerebellar volume increased 177% (from 8.25 to 22.82 mL), whereas the mean intracranial cavity volume increased 110% (from 194.7 to 410.9 mL) and mean total brain volume increased 107% (from 178.2 to 369.0 mL) during the same time period. As shown in Fig 4, cerebellar volume in these PT infants becomes a larger percentage of total brain volume. At 28 weeks, cerebellar volume averages 4.5% of total brain volume, whereas at 42 weeks, it is 7.1% of the total brain volume.

Mean cerebellar volumes of PT infants were significantly lower in those with abnormal pMRI and tMRI scans, compared with PT infants with normal scans at pMRI and tMRI (pMRI: mean 10.0 vs 12.8 mL, $P < .001$; tMRI: mean 19.7 vs 26.0 mL, $P < .001$; Fig 5). For infants with abnormal pMRI scans, cerebellar volume increased on average by 1.46 mL ($r = 0.90$, $P < .001$) for each 1-week increase in postconceptional age. Although cerebellar volume was significantly lower in PT infants with an abnormal pMRI, the rate of cerebellar growth was not statistically different in PT infants with normal versus abnormal pMRI and tMRI studies (cerebellar volume increase 1.46 vs 1.57 mL/week; $P < .05$, respectively).

Cerebellar volumes were significantly related to intracranial cavity volumes ($r = 0.91$, $P < .001$) and total brain volumes ($r = 0.92$, $P < .001$) at pMRI and tMRI studies. When the relationship between cerebellar, intracranial cavity, and total brain volumes was examined in those with normal versus abnormal pMRI (adjusting for gestational age at birth), mean cerebellar volume was 3.5 mL lower ($P < .001$) in those with abnormal versus normal pMRI, as was intracranial cavity volume (29.7 mL lower; $P < .001$) and mean total brain volume (49.6 mL lower; $P < .001$). A later postnatal age at pMRI was significantly associated with a lower cerebellar volume when controlling for postconceptional age, with an overall decrease of 0.40 mL for each 1-week increase in postnatal age ($P < .001$).

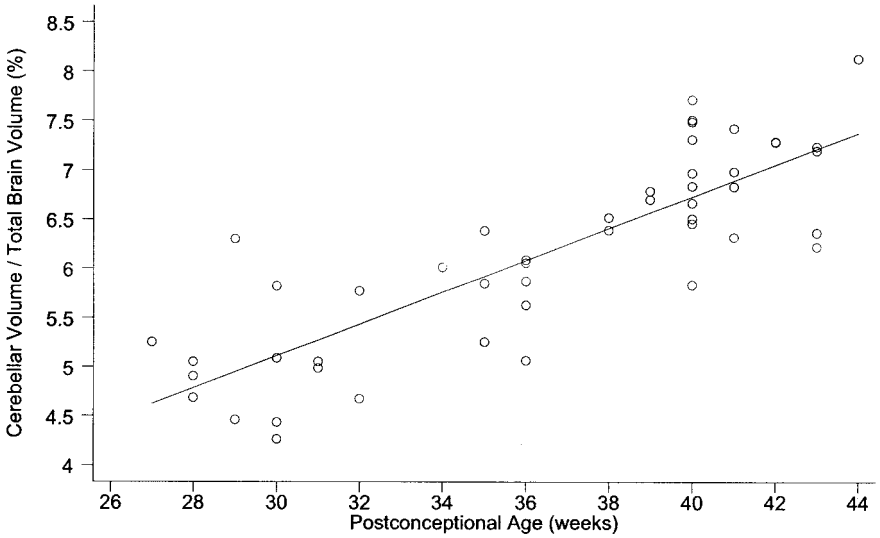

Fig 4. Cerebellar volume as a proportion of total brain volume in preterm infants with normal MRI studies.

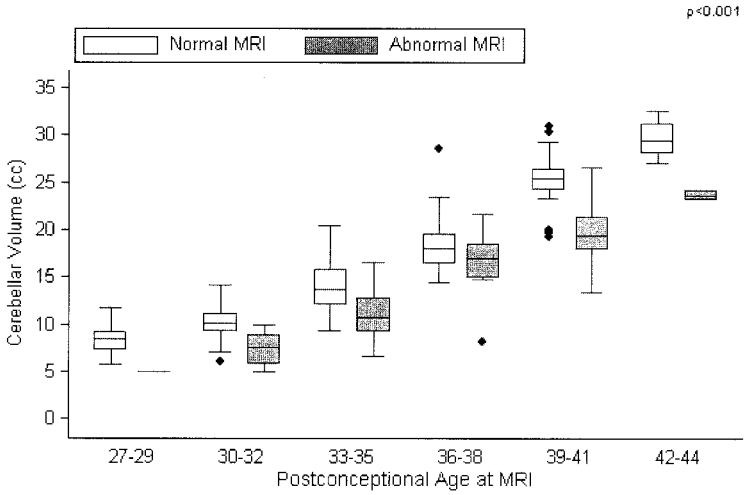

Fig 5. Relationship between cerebellar volume in preterm infants with normal and abnormal pMRI and tMRI.

Comparison of Cerebellar and Supratentorial Volumes Between PT and TB Infants at tMRI

PT infants underwent tMRI at a mean postconceptional age of 40.1 weeks. Table 3 summarizes the growth parameters of PT infants and TB infants at tMRI. PT infants with abnormal tMRI scans had a significantly reduced mean cerebellar volume (19.7 mL; $P < .001$) when compared with PT with normal tMRI scans (26.0 mL) and TB infants (27.9 mL) across all diagnostic categories. When the effects of weight and head circumference percentiles as well as postconceptional age at tMRI were adjusted for, mean cerebellar volume was lower by 3.1 mL on average for PT with normal tMRI ($P < .001$) compared with their TB peers.

The effects of the individual MRI lesions (described in Table 2) on mean cerebellar volumes of PT infants at tMRI compared with the mean cerebellar volumes in healthy TB infants were as follows: ventriculomegaly (21.8 mL), supratentorial parenchymal lesions (periventricular leukomalacia and periventricular hemorrhagic infarction; 19.9 mL), cerebellar lesions (18.3 mL), and combined supratentorial parenchymal lesions and cerebellar lesions (17.2 mL) versus healthy TB infants (27.9 mL; $P < .001$).

Predictors of Cerebellar Volume in PT Infants at tMRI

Univariate Associations

For PT infants, cerebellar volume at tMRI was significantly associated with total brain volume ($r = 0.75$, $P < .001$) and intracranial cavity volume ($r = 0.74$, $P < .001$), postconceptional age at tMRI ($r = 0.67$, $P < .001$), gestational age at birth ($r = 0.38$, $P = .002$), head circumference percentile ($r = 0.59$, $P < .001$) and weight percentile ($r = 0.53$, $P < .001$) at tMRI, and duration of mechanical ventilation ($r = -0.55$, $P < .001$). Mean cerebellar volume tended to be lower for infants with an abnormal MRI (mean: 19.7 vs 26.0 mL; $P < .001$), those who required high-frequency ventilation (mean: 20.1 vs 24.0 mL; $P = .005$), and those with a PDA (21.5 vs 24.5 mL; $P < .01$). In addition, cerebellar volume at tMRI was significantly lower for PT infants with longer hospitalization ($r = -0.51$, $P < .001$). There was no association between cerebellar volume at tMRI and singleton versus multiple gestation PT infants or gender.

Multivariate Analyses

Cerebellar volume at tMRI was larger for PT infants with larger total brain volume ($P = .005$) and

TABLE 3. Comparisons Between PT Infants at tMRI With Healthy TB Infants

Parameter	Term ($n = 20$)	Preterm Normal ($n = 37$)	Preterm Abnormal ($n = 38$)	P Value
Postconceptional age, wk, mean ± SD; median (range)	39.9 ± 0.8; 40 (38–41)	40.5 ± 1.5; 40 (38–44)	39.6 ± 1.3; 40 (38–44)	.01
Weight, g, mean ± SD; median (range)	3495 ± 288; 3573 (2948–3920)	2909 ± 550; 3125 (1390–3760)	2670 ± 483; 2640 (1310–3990)	<.001
Weight, percentile, mean ± SD	68 ± 16	42 ± 20	32 ± 18	<.001
Head circumference, cm, mean ± SD	34.8 ± 1.2	34.2 ± 1.6	32.8 ± 1.8	<.001
Head circumference, percentile, mean ± SD	71 ± 18	56 ± 22	41 ± 25	<.001
Cerebellar volume, mL, mean ± SD	27.9 ± 2.6	26.0 ± 3.7	19.7 ± 3.5	<.001
Intracranial cavity volume, mL, mean ± SD	455.2 ± 35.8	421.2 ± 60.3	372.9 ± 67.5	<.001
Total brain volume, mL, mean ± SD	430.5 ± 27.5	383.8 ± 56.4	333.1 ± 58.8	<.001
Cerebellar/intracranial cavity volume, %, mean ± SD	6.1 ± 0.3	6.3 ± 0.5	5.3 ± 0.9	<.001
Cerebellar/total brain volume, %, mean ± SD	6.5 ± 0.4	6.9 ± 0.5	6.1 ± 1.1	.001

those with higher gestational ages ($P < .001$) and smaller for infants with brain injury ($P < .001$). Together, these 3 factors explain 81% of the variability in cerebellar volume.

DISCUSSION

In this study, we demonstrate a period of rapid cerebellar growth during the period from 28 weeks' postconceptional age to term. In fact, the rate of cerebellar growth during this phase far exceeds that of the cerebral hemispheres. However, when compared with cerebellar volumes of TB infants, the cerebellum was significantly smaller in ex-preterm infants at term equivalent. This finding suggests that cerebellar development is impeded during the early weeks of premature life, even in the absence of demonstrable cerebral or cerebellar MRI injuries. Cerebellar growth restriction is amplified further by associated brain injuries, even when these are remote and confined to the supratentorial structures. Combined supratentorial and cerebellar lesions were associated with the greatest failure of cerebellar growth. Finally, we demonstrated that decreased cerebellar volume in PT infants is significantly related to gestational age at birth, birth weight, postnatal growth parameters (head circumference and weight), and risk factors related to illness severity (eg, duration of mechanical ventilation, presence of a PDA).

Quantitative MRI studies have characterized the anatomic and temporal characteristics of cerebral cortical development and myelination in PT infants between 29 and 41 weeks postconception.[5,16] Total brain tissue volume, as well as cortical gray matter and myelinated white matter volumes, has been shown to increase rapidly with increasing postconceptional age.[16] However, to our knowledge, the findings of our study represent the first description of early cerebellar growth in premature infants.

This phase of rapid cerebellar development likely represents a period of particular vulnerability in the PT infant. In fact, several lines of evidence support this notion. In late gestation, proliferation and migration of the cerebellar granule cells are particularly prominent events,[20] and insults such as hypoxia-ischemia may injure these immature granule cells, with secondary effects on other cell populations,[21] ultimately impairing cerebellar growth and development.[22,23] The premature brain is susceptible to cerebrovascular injury because of the immaturity of its vascular supply.[24] Moreover, cerebral autoregulation is underdeveloped in premature infants[25] and may be particularly deficient in the cerebellum.[26] During periods of pressure-passive cerebral perfusion, systemic hemodynamic instability will predispose to ischemic brain injury.[24] In fact, neuropathologic studies have reported a high incidence of necrotic lesions in the cerebellum of infants who are born prematurely.[27–29] Histopathologic reports in extremely premature infants with a history of severe systemic hypotension have demonstrated cystic leukomalacia in the superficial white matter of the cerebellar folia.[30] The investigators speculated that this injury may result from border-zone infarcts between the territories of the posterior inferior and superior cerebellar arteries that occur during periods of hemodynamic instability.

Existing evidence suggests that PT birth is associated with long-term, regionally specific reductions in brain volume, including the cerebellum.[2,15,31] We demonstrate for the first time that this stunted cerebellar growth in PT infants is already evident before term postconceptional age and that interventions to address this would need to be instituted very early. Our findings and those of others[2,15,31] suggest that cerebellar development is compromised in infants who are born prematurely in the presence and the absence of brain injury. However, the long-term impact of prematurity on the developing cerebellum remains to be defined.

That premature infants with isolated supratentorial injury, in our study, showed a striking and unexpected reduction in cerebellar volume, even in the absence of direct cerebellar injury, suggests an effect on cerebellar development. Severe cerebellar hypoplasia has been described qualitatively by conventional MRI studies in a small number of ex-PT children.[9,32–34] Recently, cerebellar atrophy was described in children who were born prematurely with periventricular white matter injury.[31] The cerebellum receives excitatory input from the frontoparietal cortex via the corticopontocerebellar and cerebellorubrothalamic tracts. Functional disconnection of these transneural pathways between the cerebral hemispheres and the cerebellar hemispheres may explain the phenomenon of cerebellar hypometabolism resulting in cell loss and parenchymal atrophy.[32] The immature cerebellum is presumably dependent on the transsynaptic excitatory pathways for normal growth and development.[35] Our data indicating that cerebellar growth is markedly affected in PT infants with supratentorial parenchymal lesions supports such a notion.

Our data suggest that certain perinatal risk factors predispose PT infants to impaired cerebellar growth. Among the factors that we analyzed, length of mechanical ventilation and the need for high-frequency ventilation were significantly associated with reduced cerebellar volumes in our PT cohort. The presence of a PDA was also associated with smaller cerebellar volumes in PT infants, even in the absence of brain injury. Cerebellar perfusion, particularly during diastole, may be compromised by a large PDA[36] and has been associated with border-zone infarcts of the cerebellum.[31] Cerebellar volumes were also significantly associated with head circumference and weight at tMRI. Insufficient postnatal catch-up growth in PT infants has been significantly associated with adverse neurodevelopmental outcome.[37–39] These data suggest that impaired postnatal growth may be an important marker of impaired central nervous system integrity and, in particular, deficient cerebellar growth at term.

This study has several potential limitations. Intracranial cavity and total brain volumes could not be calculated on all MRI data because of the presence of

motion artifact. However, PT infants without intracranial cavity or total brain volume measurements were not found to be different in baseline characteristics (eg, birth weight, gestational age, postconceptional age at the time of the MRI). tMRI scans were performed over a wider range of postconceptional ages for PT infants (38–44 weeks) than for healthy TB infants (38–41 weeks). Finally, the TB infants were robust overall compared with our premature infants, whose growth parameters showed greater variability. However, we did attempt to control for the potential confounding effects of gestational age at the time of the MRI as well as growth parameters in our multivariate analyses.

In summary, we have demonstrated that PT infants are at significant risk for cerebellar growth failure in the early postnatal period. Determinants of this failure of cerebellar growth in PT infants seem to be multifactorial and include lower gestational age, total brain volume, illness severity, and postnatal growth parameters including whole-brain growth. PT infants with supratentorial parenchymal lesions show a striking reduction in cerebellar volume on MRI, even in the absence of direct cerebellar injury. It is unclear whether impaired cerebellar growth is attributable to direct cerebellar injury undetected by current MRI or reflects a trophic effect from the supratentorial parenchymal lesions. At present, cerebellar impairment seems to be underappreciated in the PT infant. We speculate that impaired cerebellar growth accounts for an appreciable portion of subsequent motor, cognitive, and behavioral disabilities in PT infants. Evaluation of this possibility will require long-term neurodevelopmental follow-up studies.

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PREDICTIVE MEDICINE

"At a conference last week at Rockefeller University, sponsored by IBM, a panel of health care experts discussed the innovations that promised to be the most intriguing and the most necessary over the next decade or so. They chose 1 grand pursuit in clinical care—the probable rise of 'predictive medicine.' The idea is that advances in genetics would make it possible to know from birth a person's genetic predisposition for, say, obesity, heart disease, or cancer, and that knowledge could be used to tailor treatment or alter personal behavior. Yet the panel spent more time on the need to bring patient records and prescriptions out of the ink-and-paper era and into the computer age. 'The problem I see is that we have so much information and we need to be able to translate that information into care,' said Dr Edward D. Miller, dean of the Johns Hopkins University Medical School. . . . An estimated 31% of this year's total national healthcare bill of $41.79 trillion is spent on administration. Electronic record-keeping would eliminate enormous amounts of paper-shuffling, which could save hundreds of billions of dollars and many lives."

Lohr S. New economy. *New York Times*. November 22, 2004

Noted by JFL, MD