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Stability of Neuromotor Outcomes at 18 and 30 Months of Age After Extremely Low Birth Weight Status

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Abstract

Background—Extremely low birth weight (≤ 1000 g) children have increased rates of cerebral palsy and other abnormal neurologic findings.

Objective—To investigate the stability of neuromotor findings between 18 and 30 months' adjusted age in extremely low birth weight infants.

Methods—Seven hundred nineteen extremely low birth weight infants with assessments at 18 and 30 months' adjusted age were included in this analysis. At each visit a neurologic examination, the modified gross motor function classification system, and the Bayley Scales of Infant Development II were administered. Logistic regression models were constructed to assess neonatal factors and neuromotor function at 18 months of age associated with stability in neuromotor function.

Results—Eighty-four percent of the children had agreement in neurologic/motor function at both visits. However, classification changed from normal to abnormal in 6% and from abnormal to normal in 10%. Diagnosis of cerebral palsy was consistent for 91% of the children, and the gross motor function classification system score was consistent for 83%. In multivariate models, factors associated with decreased severity or absence of cerebral palsy diagnosis at 30 months of age were higher gestational age, no periventricular leukomalacia or severe intraventricular hemorrhage, and a gross motor function classification system score of 0 (normal) at the 18-month visit, whereas factors associated with a new cerebral palsy diagnosis at 30 months of age were postnatal steroid use, periventricular leukomalacia or severe intraventricular hemorrhage, a gross motor function classification system score of ≥ 1 at 18 months of age, and asymmetrical limb movement at 18 months of age.

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What's Known on This Subject: Survival has increased for ELBW children; however, CP and abnormal neurologic findings are at increased rates in this population. However, the stability of neurologic findings in this population by age 2 is not clear.

What This Study Adds: This study provides information on neonatal and infant characteristics that are associated with stability or worsening of neurologic findings from 18 to 30 months of age. It is important to detect early neurologic findings to provide appropriate referrals and support services.

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Conclusions—Stability of neurologic diagnosis in 84% and cerebral palsy in 91% of the children is reassuring. However, for a significant percentage of children, the neurologic diagnosis changes between 18 and 30 months of age. The diagnosis of cerebral palsy may be delayed in some infants until an older adjusted age.

Keywords

neuromotor outcomes; extreme low birth weight; prematurity; cerebral palsy

There has been an increased survival rate for extremely low birth weight (ELBW) infants (weighing ≤ 1000 g at birth); however, there are concerns that the overall prevalence of cerebral palsy (CP) is increasing among this group of infants.^{1–6} Reported prevalence rates of CP among ELBW children range between 5% and 35%.^{3–5,7}

Although many ELBW children have positive functional outcomes,^{6,8} many others have severe neurologic disability and multiple abnormal neurologic findings on clinical examination.^{3,4,8–11} The factors that help predict which children will have mild to moderate developmental delay or CP in early childhood remain unclear.^{12,13} Abnormal motor findings may change over time in preterm children.^{12,14–17} Other studies have found multiple areas of “hidden disability,” which are first identified when children reach school age.^{5,8,18–20}

A traditional neurologic examination during early infancy may fail to identify the infant with severe neurologic injury and CP. A functional assessment of movements and motor function may be a more accurate predictor.^{21–26} Improved understanding of the specific early characteristics of children later diagnosed with CP may aid in the identification of children who may benefit from additional early intervention services.^{21,22,26–29} In the United States, many neurodevelopmental outcome studies of preterm infants are performed in early infancy. Improved understanding of those findings associated with stability of motor function and diagnostic classification over time is critically important when interpreting age-specific neurodevelopmental outcome data from these studies.

The objective of this study was to investigate the stability of the motor diagnoses between 18 and 30 months' adjusted age and to investigate which characteristics are associated with changes in neuromotor diagnosis in a cohort of ELBW infants. We hypothesized that the majority of diagnoses for children with CP and/or abnormal neurologic examinations, including abnormal neuromotor functioning, would remain stable over time. Furthermore, we postulated that specific child characteristics could be identified that were associated with change in gross motor function or motor diagnosis between the 2 study visits.

Methods

Sample

This was a retrospective, longitudinal observational study. The study cohort included ELBW children enrolled in the glutamine trial³⁰ and seen both at 18 to 22 and 30 to 36 months' adjusted age. Children with a birth weight between 401 and 1000 g and cared for in 1 of the participating centers of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Neonatal Research Network from October 1999 through August 2001 were prospectively enrolled after delivery. Children with major congenital anomalies and congenital nonbacterial infection, 1 infant with a documented history of child abuse with associated traumatic brain injury, and 1 infant with a poorly healed femur fracture were excluded from the analysis. Details regarding the glutamine trial have been previously described.³⁰ The study was approved by the institutional review boards of all the centers and informed consent was obtained. There were 1433 children randomized to the study; 251 died

during the study and 26 died after discharge. One hundred twenty-one children were lost to follow-up at the 18-month visit and an additional 282 children were lost to follow-up at the 30-month visit. Overall, 90% of the survivors were followed at 18 months of age and 65% were seen at both visits. Children seen at both visits compared with children seen at 18 months of age only were less likely to have a normal neurologic examination at 18 months of age (71.6% vs 79.8%; $P[r] = .007$) and more likely to be white/non-Hispanic (40.4% vs 33.3%; $P < .010$). In addition, 14 infants with incomplete data and 20 with congenital anomalies were excluded from the analysis. This study reports the outcome of the remaining 719 infants seen at both visits with information on diagnostic classification of CP, gross motor function classification system (GMFCS) scores,²³ and neurologic status. This large cohort provides a unique opportunity to study changes of motor function over time among ELBW infants.

As part of the original protocol, data on pregnancy, delivery, and clinical outcome were prospectively obtained by trained study coordinators until 120 days after birth, transfer to another institution, hospital discharge, or death. At the follow-up visits, an interim medical history, updated social and demographic information, and anthropometric measures (weight, height, and head circumference) were obtained. Methods for establishing interrater reliability on all assessments have been reported previously.⁴ At both visits, children underwent a standardized physical and neurologic examination including the administration of the GMFCS. 7·23 Evaluators were blinded to the randomization status in the glutamine trial and were certified annually by the NICHD network. Examiners assessed tone, symmetry, reflexes, and functional gross motor skills and categorized the neurologic examination as normal or abnormal on the basis of defined criteria. Children were diagnosed as normal if there were no neurologic abnormalities present. When the results of the examination were judged abnormal, it was further described as consistent with CP or consistent with neurologic findings other than CP. The CP definition used for the NICHD network has been previously described as “a nonprogressive central nervous system disorder characterized by abnormal muscle tone in at least 1 extremity and abnormal control of movement and posture.”⁷ Coding for CP required 2 of 3 components: abnormalities observed in tone and reflexes, delay in motor milestones, and aberrations in primitive or postural reflexes. Severity of impairment was categorized as mild, moderate, or severe. Mild CP was defined as motor function that slightly interferes with but does not prevent age-appropriate motor abilities. This included nonfluent walking, asymmetric walking, exclusive or persistent toe walking with tight Achilles secondary to increased tone and brisk reflexes, and no assistive device needed for ambulating. Moderate CP was defined as motor function that interferes with age-appropriate motor activities. The child can sit independently or with trunk support required for floor sitting but does not ambulate or use assistive devices. Severe CP was defined as significant impairment in motor function characterized by no ambulation, no sitting, and no supported sitting.

The GMFCS describes the level of a child's gross motor performance, and it has been previously described.^{7·23} GMFCS scores range from 0 for normal to 5 for most impaired. In addition, certified examiners administered the Bayley Scales of Infant Development II.³¹ A Mental Developmental Index (MDI) and Psychomotor Developmental Index (PDI) corrected for gestational age were derived. A score of <70 is 2 SDs below the mean. Children who scored <50 on the MDI or PDI or who could not be tested because of severe developmental delay were assigned a score of 49.

Outcome Measures

The outcome measures used for this study were neurologic status (normal versus abnormal), CP (mild, moderate, or severe versus no CP), and functional status on the GMFCS (abnormal score of ≥ 1 versus normal score of 0).

Analysis

RTI International assessed data completion, consistency, and performed all data analyses. Data analysis was performed by using SAS 9.1 (SAS Institute, Inc, Cary, NC). Student's t and χ^2 tests were used for initial bivariate analyses. Logistic regression models were constructed by using a modified backward selection method, and only significant variables were retained in the final models. Neonatal variables screened were gestational age at birth, severe intraventricular hemorrhage (IVH) (3–4) and/or periventricular leukomalacia (PVL), bronchopulmonary dysplasia, retinopathy of prematurity, necrotizing enterocolitis, use of postnatal steroids in the nursery, gender, and race (white versus nonwhite). Variables from the 18-month examinations included z scores for weight to length and head circumference, GMFCS scores (normal versus abnormal), MDI or PDI scores of <70 , ≥ 1 joint with clonus or increased deep tendon reflexes (DTR), at least 2 limbs with abnormal muscle tone, and asymmetric limb movement. Abnormal tone was defined as suspect or definite increased/decreased tone or varying tone. Asymmetry was defined as upper or lower limb asymmetry. Other independent variables were caretaker marital status and household socioeconomic score (SES).

Because we were interested in agreement of diagnoses over time at both visits, we used the κ coefficient, for which a value of 1 represents complete agreement and 0 represents a chance agreement. For diagnosis with multiple categories, we used a weighted κ coefficient, which takes into account how far apart the diagnoses are if they do not agree. The positive and negative predictive values (PPVs and NPVs) associated with the ability to predict 30-month outcomes based on the 18-month assessment were also calculated. For each outcome, the PPV was defined as the number of children with abnormal results at 30 months of age divided by the total number with abnormal results at 18 months of age. Similarly, the NPV was defined as the number of children with normal results at 18 months of age divided by the total number with normal results at 30 months of age.

Results

Stability of findings between the 2 study visits is presented in Table 1. The children are categorized into 4 groups on the basis of their neuromotor examinations at 18 and 30 months of age: normal at both ages, abnormal at both ages, classification changed from normal to abnormal, or classification changed from abnormal to normal.

Overall Neurologic Examination

Of the 719 ELBW children who had a neurologic examination at 18 and 30 months of age, 477 (66%) remained normal and 128 (18%) remained abnormal ($\kappa = 0.59$) (see Tables 1 and 2). Of the 114 children who changed their diagnoses over time, 45 changed from a normal neuromotor examination at 18 months of age to an abnormal examination at 30 months of age, and 69 changed from an abnormal examination at 18 months of age to a normal neuromotor examination at 30 months of age. Thus, the PPV of an abnormal overall neurologic examination at 18 months of age for an abnormal neurologic examination at 30 months of age was 65% (128 of 197), and the NPV of a normal neurologic examination at 18 months of age for a normal neurologic examination at 30 months of age was 91% (477 of 522).

Cerebral Palsy

As shown in Table 1, 599 (83%) children did not have CP at either visit, and 67 (9%) children were diagnosed with CP at both study visits ($\kappa = 0.67$). Stability of a diagnosis of moderate to severe CP had a κ value of 0.74. Fifty-five (8%) children were diagnosed with the same severity of CP at both examinations, and 65 (9%) children had a change in CP diagnosis between

examinations. Thirty (4%) children improved to a diagnosis of no CP, and 30 (4%) had either newly diagnosed CP or an increase in severity of CP.

As shown in Table 2, among children who were classified as having an abnormal neurologic examination but not CP at 18 months of age, 18 (18%) of 100 were subsequently classified as having CP at 30 months of age (11 mild, 6 moderate, and 1 severe) and 49 (49%) of 100 had a normal neurologic examination at 30 months of age. Among children who were classified as having an abnormal neurologic examination but no CP at 30 months of age, 10 (12%) of 83 had previously been classified with CP at 18 months of age. Among the children who were not classified as having CP at 18 months of age, 23 (4%) of 622 had the diagnosis at 30 months of age. Of the children with a classification of CP at 18 months of age, 30 (31%) of 97 were not classified as having CP at 30 months of age; however, 20 (67%) of 30 had abnormal neuromotor findings at 30 months of age and 10 (33%) of 30 were normal at 30 months of age.

A classification of CP at 18 months of age had a 69% (67 of 97) PPV for a diagnosis of CP at 30 months of age. Conversely, not having a classification of CP at 18 months of age had a 96% (599 of 622) NPV for not being classified as having CP at 30 months of age.

Gross Motor Function Scores

The modified GMFCS score was the same at both visits for 595 (83%) of the children evaluated (weighted $\kappa = 0.67$), which suggests that the neurologic and functional examinations demonstrated good stability of findings between the 18- and 30-month examinations (Table 1).

Although the majority of children had a stable classification, 124 (17%) children changed their GMFCS status between examinations. In examining the changes in the modified GMFCS scores, the greatest numbers of children who changed were categorized at 18 months of age as possible level 1 (46 children) or level 1 (36 children). These 2 levels of the GMFCS represent mild gross motor delays (Table 3).

Factors Associated With Change and Stability of Neurologic Status, CP, and GMFCS

Using logistic regression models (Tables 4 and 5) to assess the stability of the neurologic examination, a PDI score of < 70 at 18 months of age was associated with a change from normal examination at 18 months of age to an abnormal neurologic examination at 30 months of age. A PDI score of > 70 was associated with a change from abnormal neurologic status at 18 months of age to normal at 30 months of age. Other factors associated with improvement were absence of clonus or increased DTR at the 18-month assessment, absence of PVL or severe IVH, and not having received postnatal steroids.

Logistic regression model results showed that children who received a new diagnosis of CP at 30 months of age were more likely to have received postnatal steroids, to have severe IVH or PVL, to have a GMFCS score of ≥ 1 at 18 months of age, and to have asymmetrical limb movement at 18 months of age (Table 6). Children who were classified as having CP at 18 months of age but had improved at 30 months of age were more likely to have higher gestational ages, a GMFCS score of 0 at 18 months of age, and were less likely to have severe IVH or PVL.

In logistic regression analysis, children with a GMFCS score of 0 at 18 months of age who had a score ≥ 1 at 30 months of age were more likely to have severe IVH, PVL, or necrotizing enterocolitis, or abnormal muscle tone in ≥ 2 extremities at 18 months of age (Table 7).

Children with an abnormal GMFCS score at 18 months of age who improved their score at 30 months of age were more likely to have a MDI score of ≥ 70 at the 18-month examination,

abnormal muscle tone in fewer than 2 limbs at the 18-month examination, and a lower household SES. They were less likely to have a history of severe IVH or PVL.

Discussion

In contrast to previous studies that documented change in classification of neurologic findings in ELBW children between infancy and preschool, the majority of children in our cohort demonstrated stability of neuromotor classification and functional status between assessments performed at 18 and 30 months' adjusted age.^{12,14,15} We believe this stability is due in part to the use of network-certified examiners who participated in training and yearly recertification. The children were reexamined primarily in the same center at 18 and 30 months of age. The resolving of some neurologic findings and the emergence of new neurologic findings is known to occur. Therefore, the combination of a functional tool like the modified GMFCS with the neurologic examination may improve early diagnoses.^{7,32,33} In our study, a normal GMFCS score at 18 months of age was associated with stability of normal neurologic findings, and a higher GMFCS score was associated with a subsequent diagnosis of CP, or lack of improvement in previously diagnosed CP, at the 30-month visit. The modified GMFCS is a simple reliable tool that could be administered by other noncertified examiners and has been recommended in the new classification of CP.^{23,34}

Agreement of classification of CP at the 18- and 30-month visit was moderate and was higher when we combined moderate to severe CP versus mild CP or no CP. This has been observed previously by others.³² However, it is important to identify both nondisabling and disabling CP, because even mild CP will impact the quality of life of a growing child.^{8,27}

Several neonatal morbidities have been studied previously regarding their association with neurologic outcomes in ELBW populations.^{4,35,36} We found that the presence of severe IVH or PVL was associated with a new diagnosis of CP at 30 months of age for infants undiagnosed at 18 months of age, as well as a lack of improvement in CP for those diagnosed at 18 months of age. Similarly, the presence of severe IVH or PVL was also associated with a change from normal to abnormal GMFCS scores between 18 and 30 months of age and a lack of improvement at 30 months of age for those with an abnormal score at 18 months of age. Consistent with those findings, PVL or severe IVH was also associated with having an abnormal neurologic examination at both visits. Thus, PVL or severe IVH was a consistent morbidity associated with a worsening examination and should be considered when examining the ELBW child at 18 to 22 months of age relative to prognosis and referral for early intervention.

Having received postnatal steroids was associated with an abnormal neurologic examination at both 18 and 30 months of age as well as a new diagnosis of CP at 30 months of age. Necrotizing enterocolitis was associated with a change from normal to abnormal GMFCS scores between 18 and 30 months of age. The only other neonatal characteristic that was significant in the logistic regression models was higher gestational age, which was associated with decreased severity of CP between the 2 visits.

Several components of the neuromotor examination at 18 months of age were associated with instability of findings at 30 months of age. Children with asymmetry at 18 months of age had 4 times the odds of having a new diagnosis of CP at 30 months of age compared with children who did not have asymmetry. Several authors have emphasized infant movements and asymmetry as predictors of CP.³⁷ Other important neurologic signs include the presence of clonus or increased DTRs in ≥ 1 joints at 18 months of age, which was associated with persistent abnormal examination at 30 months of age. Tone is an important component of the neurologic examination and is used frequently for diagnosis of CP. We found that abnormal muscle tone

in ≥ 2 limbs was associated with a lack of improvement in GMFCS scores at 30 months of age for children with abnormal GMFCS scores at 18 months of age, as well as having an abnormal score at 30 months of age for children who had a normal score at 18 months of age. This is consistent with previous findings that early normal tone predicts a normal neuromotor examination at 36 months' adjusted age.¹² Abnormal tone, however, was not found to be associated with stability of diagnosis of CP between 18 and 30 months of age; this could be secondary to transient dystonias found in ELBW children.^{12,16}

With regard to the Bayley Scales of Infant Development II scores, a PDI score of ≥ 70 at 18 months of age was associated with a stable normal neurologic examination, as well as improvement of the neurologic examination over time. In addition, children who demonstrated an improvement in their gross motor function classification score were more likely to have a MDI score of ≥ 70 at 18 to 22 months of age. This may be a reflection of greater central nervous system integrity, particularly because infants who improved were also less likely to have a history of PVL or severe IVH. Socioeconomic factors included in the models were not consistently associated with neurologic outcomes. Low SES was associated with greater improvement of GMFCS scores between 18 and 30 months of age. Other unmeasured factors could be associated with these findings including post discharge illness, nutrition, poverty, and timing and access to early intervention services. There is some indication that children with abnormal GMFCS scores at 18 months of age tended to have a lower household SES (median scores test: $P = .09$), which may be a contributing factor.

This study has several limitations. The examiners for the 30-month assessment were not consistently blinded to the 18-month examination results or the neonatal history.³⁸ However, our study demonstrated consistent neurologic findings in children 18 to 30 months of age. Examiners were certified yearly and children were seen mostly at the same center. However, it may have been better if same examiner did both examinations.

The role of early intervention, including occupational or physical therapy, was collected comprehensively, but no information was available on duration or intensity of therapy. In addition, it is not possible to assess the effects of intervention retrospectively, because children with greater impairments are more likely to receive services. Therefore, these variables were not included in the analysis.

Conclusions

The follow-up examinations given to children enrolled demonstrated good stability of neurologic diagnoses between the ages of 18 and 30 months of age. Characteristics measured at 18 months of age associated with abnormal or worsening of findings at 30 months of age were (1) asymmetrical limb movement, (2) ≥ 2 limbs with abnormal muscle tone, (3) a PDI or MDI score of < 70 , (4) ≥ 1 joint with clonus or increased DTR, and (5) a GMFCS score of ≥ 1 . Knowledge of neurologic and gross motor findings and Bayley scores associated with persistent or emergent neurologic abnormalities provides guidance to the examiner in determining appropriate referrals and support services.

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Abbreviations

ELBW	extremely low birth weight
CP	cerebral palsy
GMFCS	gross motor function classification system
MDI	Mental Developmental Index
PDI	Psychomotor Developmental Index
NICHD	Eunice Kennedy Shriver National Institute of Child Health and Human Development
NPV	negative predictive value
PPV	positive predictive value
DTR	deep tendon reflexes
SES	socioeconomic score
IVH	intraventricular hemorrhage
PVL	periventricular leukomalacia

TABLE 1
Overall Stability of Diagnoses of ELBW Children From the 18-Month to the 30-Month Visit

Outcome	Remained Same, Normal, <i>n</i> (%)	Worsened From Normal to Abnormal, <i>n</i> (%)	Worsened From Abnormal to More Abnormal, <i>n</i> (%)	Improved From Abnormal to Less Abnormal, <i>n</i> (%)	Improved From Abnormal to Normal, <i>n</i> (%)	Remained Same, Abnormal, <i>n</i> (%)	Coefficient for Agreement, κ (CI)
Neurologic examination	477 (66)	45 (6)			69 (10)	128 (18)	0.59 (0.52–0.65)
Diagnosis of CP	599 (83)	23 (3)	7 (1)	5 (1)	30 (4)	55 (8)	0.71 (0.64–0.79) ^a
Diagnosis of moderate to severe CP ^b	671 (93)	12 (2)			7 (1)	29 (4)	0.74 (0.63–0.85)
GMFCS	548 (76)	17 (2)	25 (3)	21 (3)	61 (8)	47 (7)	0.67 (0.61–0.73) ¹
GMFCS score ≥ 1 ^c	548 (76)	17 (2)			61 (8)	93 (13)	0.64 (0.57–0.71)

CI indicates confidence interval.

^aWeighted κ coefficient.

^bNormal refers to not having moderate or severe CP; therefore, mild CP may be included in the normal category.

^cGMFCS score ≥ 1 versus score of 0 (normal).

TABLE 2
Overall Changes in Neurologic and CP Classification

Neuromotor Examination at 18 mo	Neuromotor Examination at 30 mo, <i>n</i> (%)						
	Normal	Abnormal, Not CP	Total CP	Mild CP	Moderate CP	Severe CP	Total
Normal	477 (66)	40 (6)	5 (1)	5 (1)	0 (0)	0 (0)	522 (73)
Abnormal, not CP	49 (7)	33 (5)	18 (3)	11 (2)	6 (1)	1 (0)	100 (14)
Total CP	20 (3)	10 (1)	67 (9)				97 (13)
Mild CP	20 (3)	8 (1)		28 (4)	5 (1)	0 (0)	61 (8)
Moderate CP	0 (0)	1 (0)		5 (1)	15 (2)	2 (0)	23 (3)
Severe CP	0 (0)	1 (0)		0 (0)	0 (0)	12 (2)	13 (2)
Total	546 (76)	83 (12)	90 (13)	49 (7)	26 (4)	15 (2)	719 (100)

TABLE 3

Overall Changes in Neurologic and GMFCS Classification

GMFCS at 18 mo	GMFCS at 30 mo, <i>n</i> (%)						Total, <i>n</i> (%)
	0 = Normal	Possible Level 1	Level 1	Level 2	Level 3	Level 4	Level 5
0 = normal	548 (76)	11 (2)	6 (1)	0 (0)	0 (0)	0 (0)	0 (0)
Possible level 1	37 (5)	15 (2)	9 (1)	0 (0)	0 (0)	0 (0)	0 (0)
Level 1	22 (3)	9 (1)	14 (2)	5 (1)	0 (0)	0 (0)	0 (0)
Level 2	1 (0)	6 (1)	3 (0)	13 (2)	1 (0)	1 (0)	0 (0)
Level 3	1 (0)	0 (0)	0 (0)	2 (0)	2 (0)	2 (0)	1 (0)
Level 4	0 (0)	0 (0)	0 (0)	0 (0)	1 (0)	2 (0)	6 (1)
Level 5	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0)
Total	609 (85)	41 (6)	32 (4)	20 (3)	4 (1)	5 (1)	8 (1)
							719 (100)

TABLE 4
Characteristics of the Study Group, Categorized According to Neurologic Examination Outcome

	Stable/Remained Normal	Unstable/Worsened From Normal to Abnormal	Unstable/Improved From Abnormal to Normal	Stable/Remained Abnormal	P
<i>n</i> (%)	477 (71)	45 (5)	69 (8)	128 (16)	
Gestational age, mean $\pm$ SD, wk	26.7 $\pm$ 1.8	26.2 $\pm$ 1.7	26.4 $\pm$ 1.9	26.1 $\pm$ 1.9	.0058
Birth weight, mean $\pm$ SD, g	803.4 $\pm$ 124	765.3 $\pm$ 123	764.5 $\pm$ 135	758.3 $\pm$ 141	.0006
Multiple birth, <i>n</i> (%)	94 (19.7)	12 (26.7)	20 (29.0)	26 (20.3)	.2601
Gender, male, <i>n</i> (%)	195 (40.9)	25 (55.6)	32 (46.4)	66 (51.6)	.0594
Race, <i>n</i> (%)					.0202
Black, non-Hispanic	206 (43.2)	24 (53.3)	30 (43.5)	65 (50.8)	
White, non-Hispanic	198 (41.5)	16 (35.6)	22 (31.9)	52 (40.6)	
Hispanic	66 (13.8)	4 (8.9)	12 (17.4)	10 (7.8)	
Other	7 (1.5)	1 (2.2)	5 (7.3)	1 (0.8)	
Bronchopulmonary dysplasia (O ₂ at 36 wk), <i>n</i> (%)	191 (40.0)	21 (46.7)	38 (55.1)	80 (62.5)	<.0001
PVL or IVH grade 3–4, <i>n</i> (%)	40 (8.4)	4 (9.1)	6 (8.7)	39 (30.5)	<.0001
Neurotizing enterocolitis, <i>n</i> (%)	37 (7.8)	2 (4.4)	9 (13.0)	13 (10.2)	.3106
Early-onset sepsis, <i>n</i> (%)	2 (0.4)	2 (4.4)	2 (2.9)	—	.0053
Postnatal steroids, <i>n</i> (%)	133 (27.9)	14 (31.1)	24 (34.8)	70 (54.7)	<.0001
SES, mean $\pm$ SD	35.0 $\pm$ 13.6	33.5 $\pm$ 12.4	31.6 $\pm$ 12.6	34.1 $\pm$ 13.7	.2632
Bayley PDI score at 18 mo, mean $\pm$ SD	91.8 $\pm$ 14.2	85.8 $\pm$ 17.2	76.8 $\pm$ 15.6	62.2 $\pm$ 16.5	<.0001
Bayley PDI score at 30 mo, mean $\pm$ SD	91.7 $\pm$ 17.7	77.6 $\pm$ 19.3	77.9 $\pm$ 19.8	61.2 $\pm$ 17.2	<.0001
CP at 30 mo, <i>n</i> (%)					<.0001
None/normal	477 (100)	40 (88.9)	69 (100)	43 (33.6)	
None/neurologic other	0 (0.0)	5 (11.1)	0 (0.0)	44 (34.4)	
Mild	0 (0.0)	0 (0.0)	0 (0.0)	26 (20.3)	
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	15 (11.7)	
Severe					
GMFCS score $\geq$ 1 at 30 mo	3 (0.6)	7 (15.6)	1 (1.5)	99 (77.3)	<.0001

TABLE 5
Logistic Regression Models for Factors Associated With Stability of Neurologic Examination

Variables That Were Significant	Normal at Both Ages		Abnormal Neurologic at Both Ages		Normal at 18 mo to Abnormal Neurologic at 30 mo		Abnormal Neurologic at 18 mo to Normal at 30 mo	
	Model (N = 488)		Model (N = 180)		Model (N = 488)		Model (N = 180)	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
IVH 3–4 or PVL	NS		4.23	1.43–12.54	NS		0.24	0.08–0.70
Bayley PDI score <70 at 18 mo	0.200	0.08–0.52	4.01	1.94–8.28	4.90	1.91–12.58	0.25	0.12–0.52
Postnatal steroids	NS		2.29	1.11–4.72	NS		0.44	0.21–0.90
≥1 joint with clonus or increased DTR at 18 mo	NI		11.35	1.39–92.79	NI		0.09	0.01–0.72
GMFCS score ≥1 at 18 mo	NS		NS		6.23	2.50–15.51	NS	

Models include all subjects with nonmissing values for variables. Additional variables that did not reach statistical significance and therefore were not included in the final model were: ≥2 limbs with abnormal muscle tone at 18 months of age, MDI score of <70 at 18 months, z scores for weight for length and z scores for head circumference at 18 months, gestational age, gender, race, caretaker married, SES, necrotizing enterocolitis, bronchopulmonary dysplasia, and retinopathy of prematurity. Asymmetry and abnormal tone were not included in models for infants with normal neurologic examination at 18 months because of an insufficient number of infants with those characteristics. OR indicates odds ratio; NS, not significant and not included in the final model; NI, not included in model because of insufficient number of infants with characteristic.

TABLE 6
Logistic Regression Models for Factors Associated With Stability of CP Diagnosis

Variables That Were Significant	No CP at Both Ages		CP Does Not Improve		No CP at 18 mo to CP at 30 mo		CP at 18 mo to Improved CP or No CP at 30 mo	
	Model (N = 614)		Model (N = 97)		Model (N = 614)		Model (N = 97)	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Higher gestational age, wk	NS		0.73	0.5–0.96	NS		1.38	1.04–1.82
IVH 3–4 or PVL	0.27	0.09–0.77	6.42	1.61–25.59	3.77	1.30–10.94	0.16	0.04–0.62
Postnatal steroids	0.33	0.13–0.89	NS		3.00	1.13–7.97	NS	
Asymmetry at 18 mo	0.26	0.07–0.96	NS		3.81	1.04–13.94	NS	
GMFCS score ≥ 1 at 18 mo	0.12	0.04–0.32	16.13	1.49–175.26	8.37	3.10–22.59	0.06	0.01–0.67

Models include all subjects with nonmissing values for variables. Additional variables that did not reach statistical significance and therefore were not included in the final model were: ≥ 2 limbs with abnormal muscle tone at 18 months of age, ≥ 1 joint with clonus or increased DTR at 18 months, MDI score of < 70 at 18 months, PDI score of < 70 at 18 months, z scores for weight for length and z scores for head circumference at 18 months, gender, race, caretaker married, SES, necrotizing enterocolitis, bronchopulmonary dysplasia, and retinopathy of prematurity. Abnormal tone was not included for children who had CP at 18 months, and clonus was not included for infants without CP at 18 months, because nearly all infants had the same value for the predictor.

TABLE 7
Logistic Regression Models for Factors Associated With Stability of Gross Motor Function Classification

Variables That Were Significant	GMFCS Score Normal Both Ages		GMFCS Score Does Not Improve		GMFCS Score Normal at 18 mo to ≥ 1 at 30 mo		GMFCS Score Improves From 18 mo to 30 mo	
	Model (N = 561)	95% CI	Model (N = 144)	95% CI	Model (N = 561)	95% CI	Model (N = 144)	95% CI
IVH 3–4 or PVL	OR 0.25	0.07–0.86	OR 3.77	1.52–9.36	OR 3.99	1.16–13.69	OR 0.27	0.11–0.66
Abnormal tone in ≥ 2 limbs at 18 mo	0.12	0.04–0.32	5.35	2.10–13.62	8.53	3.08–23.63	0.19	0.07–0.48
Necrotizing enterocolitis	0.25	0.07–0.86	NS		4.03	1.16–13.97	NS	
Bayley MDI score < 70 at 18 mo	NS		2.83	1.25–6.39	NS		0.35	0.16–0.80
Lower household SES	NS		0.96	0.93–0.99	NS		1.05	1.01–1.08

Models include all subjects with nonmissing values for variables. Additional variables that did not reach statistical significance and therefore were not included in the final model were: PDI score of < 70 at 18 months of age, asymmetry at 18 months, ≥ 1 joint with clonus or increased DTR at 18 months, z scores for weight for length and z scores for head circumference at 18 months, gestational age, gender, race, caretaker married, SES, postnatal steroids, necrotizing enterocolitis, bronchopulmonary dysplasia, and retinopathy of prematurity. Clonus and asymmetry were excluded from models for infants with a normal GMFCS score at 18 months because of low incidence.