ARTICLE

Predicting Motor Development in Very Preterm Infants at 12 Months' Corrected Age: The Role of Qualitative Magnetic Resonance Imaging and General Movements Assessments

Alicia J. Spittle, MPhysio, BAppSc[a,b,c,d], Roslyn N. Boyd, PhD, MSc, BAppSc, BSc[c,e], Terrie E. Inder, MBChB, MD[a,f], Lex W. Doyle, MD, FRACP[a,c,d,g]

[a]Victorian Infant Brain Studies, Murdoch Childrens Research Institute, Melbourne, Australia; [b]School of Physiotherapy, Departments of [c]Pediatrics and [g]Obstetrics and Gynecology, University of Melbourne, Melbourne, Australia; [d]Royal Women's Hospital, Melbourne, Australia; [e]Queensland Cerebral and Rehabilitation Research Center, University of Queensland, Queensland, Australia; [f]Departments of Pediatrics, Neurology and Radiology, St Louis Children's Hospital, Washington University, St Louis, Missouri

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What's Known on This Subject

WMA and GMs assessment have been shown to be predictive of outcome at later ages. However, there is little known about their predictive value for detecting motor dysfunction in preterm infants at 1 year.

What This Study Adds

This study is the first to compare the validity of qualitative MRI and GMs assessment for predicting motor dysfunction, including cerebral palsy for preterm infants at 1 year of age. This is important for infants who do not have access to MRI.

ABSTRACT

OBJECTIVE. The objective of this study was to compare the predictive value of qualitative MRI of brain structure at term and general movements assessments at 1 and 3 months' corrected age for motor outcome at 1 year's corrected age in very preterm infants.

PATIENTS AND METHODS. Eighty-six very preterm infants (<30 weeks' gestation) underwent MRI at term-equivalent age, were evaluated for white matter abnormality, and had general movements assessed at 1 and 3 months' corrected age. Motor outcome at 1 year's corrected age was evaluated with the Alberta Infant Motor Scale, the Neuro-Sensory Motor Development Assessment, and the diagnosis of cerebral palsy by the child's pediatrician.

RESULTS. At 1 year of age, the Alberta Infant Motor Scale categorized 30 (35%) infants as suspicious/abnormal; the Neuro-Sensory Motor Development Assessment categorized 16 (18%) infants with mild-to-severe motor dysfunction, and 5 (6%) infants were classified with cerebral palsy. White matter abnormality at term and general movements at 1 and 3 months significantly correlated with Alberta Infant Motor Scale and Neuro-Sensory Motor Development Assessment scores at 1 year. White matter abnormality and general movements at 3 months were the only assessments that correlated with cerebral palsy. All assessments had 100% sensitivity in predicting cerebral palsy. White matter abnormality demonstrated the greatest accuracy in predicting combined motor outcomes, with excellent levels of specificity (>90%); however, the sensitivity was low. On the other hand, general movements assessments at 1 month had the highest sensitivity (>80%); however, the overall accuracy was relatively low.

CONCLUSION. Neuroimaging (MRI) and functional (general movements) examinations have important complementary roles in predicting motor development of very preterm infants. *Pediatrics* 2009;123:512–517

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Key Words
cerebral palsy, motor development, MRI, neonatal, premature infants

Abbreviations
PVL—periventricular leucomalacia
WMA—white matter abnormality
GMs—general movements
AIMS—Alberta Infant Motor Scale
NSMDA—Neuro-Sensory Motor Developmental Assessment
CI—confidence interval

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Address correspondence to Alicia Spittle, MPhysio, BAppSc, Victorian Infant Brain Studies, Murdoch Children's Research Institute, 2nd Floor, Royal Children's Hospital, Flemington Road, Parkville 3052, Melbourne, Australia. E-mail: alicia.spittle@rch.org.au

PRETERM BIRTHS BEFORE 30 weeks' gestation are increasing because of many factors, including assisted reproduction, multiple births, and women aged >34 years giving birth.[1] With advances in perinatal medicine over the past decades, survival rates for preterm infants have improved considerably. However, these preterm survivors remain at risk for a complex range of motor, cognitive, sensory, behavioral, and health problems compared with children born at term.[2,3]

Brain injury during the perinatal period is the most common cause of morbidity for preterm infants.[4] These brain injuries are often caused by multiple lesions and can include germinal matrix intraventricular hemorrhage, posthemorrhagic hydrocephalus, and periventricular leucomalacia (PVL).[5] The presence of cystic PVL, which consists of

focal necrotic lesions, evolving to cysts, is highly predictive of cerebral palsy and occurs in ~3% to 4% of surviving very preterm infants.[5,6] Perhaps of greater concern is the high frequency of diffuse noncystic white matter abnormalities (often referred to as diffuse PVL or white matter abnormality [WMA]), which have also been shown to be predictive of later neurodevelopmental impairments in very preterm infants.[7] Diffuse WMA consists principally of MRI signal change, often accompanied by ventricular dilation and white matter atrophy, and is the most common brain alteration seen in preterm infants by term equivalent.[7–10] Such alterations have been shown to be poorly detected on cranial ultrasound, limiting the potential of cranial ultrasound in predicting outcomes.[11,12] However, although MRI is superior in its delineation of WMA and prediction of outcomes, it is limited in its accessibility for some preterm infants and thus it would be valuable to have functional assessment tools that may be prognostic and available at the bedside. In addition, the combination of both a functional assessment tool and a tool that assesses brain structure (MRI) may lead to greater precision in predicting those infants who are at risk of motor impairments. Prechtl's method of assessing spontaneous movements in infants, known as general movements (GMs) assessments, are reported to be more valid than neurologic examination and cranial ultrasound in predicting the long-term outcome of preterm infants.[13] GMs assessments have greater sensitivity in predicting cerebral palsy than other motor assessments that can be used in early infancy.[14]

Thus, the objective of this study was to compare qualitative MRI of brain structure at term-equivalent age and GMs assessments at 1 and 3 months' corrected age in predicting motor outcome at 1 year's corrected age in very preterm infants.

METHODS

Participants

All very preterm infants born at less than <30 weeks' gestation between January 2005 and September 2006 at the Royal Women's Hospital (Melbourne, Australia) or transferred there shortly after were eligible for this study. Because the study involved home-based assessment, families needed to be living within a 100-km radius of the hospital. Families needed to speak English, because funding was not available for interpreters. Infants were excluded if they were still in hospital at 4 weeks' corrected age or had a major congenital abnormality associated with early mortality. The study was approved by the Royal Women's Hospital and Royal Children's Hospital research and ethics committees.

Procedure for MRI

MRI was performed at term-equivalent age (38–44 weeks' postmenstrual age) at the Royal Children's Hospital, Melbourne, Australia. The infants were fed, fitted with earmuffs to minimize noise exposure, then carefully wrapped and placed in a vacuum fixation beanbag (S&S Radiographic Products, Brooklyn, NY) designed to keep the infant still and supported in the scanner.[7] All imaging was obtained without sedation or anesthesia. MRI was performed by using a 1.5-T General Electric Signa System (General Electric-Medical Systems, Milwaukee, WI) on the first 51 infants, and the remaining infants were scanned using a 3.0-T Siemens Trio (software versions 11b and 13b) using previously published sequences.[15]

A standardized qualitative structural scoring system was used to qualitatively assess WMA.[11,16] All scans were scored independently by a pediatric neuroradiologist or neonatologist without previous knowledge of clinical status. This method has been reported to have excellent predictive validity and reliability.[7] WMA was graded by using 5 items including (1) the nature and extent of white matter signal abnormality, (2) periventricular white matter volume loss, (3) the presence of any cystic abnormalities, (4) ventricular dilatation, and (5) thinning of the corpus callosum. WMA was then further classified by the composite scores of these 5 categories (potential range in scores: 5–15) to no injury (score: 5–6), mild (score 7–9), moderate (score 10–12), or severe (score 13–15) abnormality.[6]

Procedure for GMs

Videotaped recordings of GMs were obtained on 2 occasions. The first was at 1 month (range: ±1 week) postterm, and the second at 3 months (range: ±1 week) corrected. One month was chosen for the first assessment because it has been shown to have greater sensitivity and specificity than term age in preterm infants.[13] Three months was chosen as the time point to assess fidgety movements because they peak at ~3 months' corrected age.[17] The infants were videoed in their homes, lying supine during periods of alert wakefulness, wearing minimal clothing. The GMs were classified as normal or abnormal according to the gestalt-perception of the global quality of the movement pattern.[18–20] At 1 month, writhing GMs were described as normal or abnormal (poor repertoire, cramped synchronized, or chaotic). At 3 months, GMs of a fidgety nature were described as normal, abnormal, or absent.[20,21] Trajectories for each infant were then described with an infant classified as having a normal trajectory if they received a score of normal at both 1 and 3 months, transient abnormal GMs trajectory if they received a score of abnormal at 1 month followed by a normal score at 3 months, or consistently abnormal trajectory if they scored abnormal at 1 month and abnormal/absent at 3 months. The quality of GMs was rated from video recordings by an assessor blinded to MRI results. At both time points, 20–30 minutes of video footage was acquired.

Procedure for Outcome Assessments

At 12 months' corrected age, all infants' motor development was assessed with both the Alberta Infant Motor Scale (AIMS)[22] and Neuro-Sensory Motor Developmental Assessment (NSMDA)[23] by a rater masked to previous assessment results. A standardized assessment technique was used according to the AIMS and NSMDA manuals.[22,23] Toys and interaction with parents and therapists

were used to encourage optimal motor performance. Minimal handling was required to facilitate the infant into the required positions. The AIMS is a gross motor assessment, which involved observing the infant in prone, sitting, supine, and standing positions. A total raw score is calculated and a percentile rank given based on a sample of 2202 infants from Alberta, Canada. A score which was equal or below the fifth centile scores published in the AIMS manual was used to classify infants' motor development as suspicious/abnormal at 12 months of corrected age. The NSMDA includes 6 subscales: gross motor, fine motor, neurologic, primitive reflexes, postural reactions, and sensorimotor responses.[24] The test is criterion referenced, with the performance of a child measured against a set of predetermined criteria that are designed to assess the quality of performance, as well as age-appropriate task achievement.[24] Results from each of the 6 subscales are added together to give a total raw score. In addition, a functional classification of normal, minimal, mild, moderate, severe, or profound motor dysfunction is obtained on the basis of the child's performance and the therapist's judgment of function in each of the 6 subscales. Cerebral palsy was diagnosed by the child's treating pediatrician.

Statistical Analysis

Data were analyzed by using Stata 10 (Stata Corp, College Station, TX). Correlations between WMA (nil to mild versus moderate to severe) and GMs (normal versus abnormal) at 1 and 3 months with the AIMS classification (normal versus suspicious/abnormal) and NSMDA classification (normal, minimal, mild, moderate, severe, or profound) at 12 months' corrected age were assessed by using Spearman's rank correlation coefficient (r). In addition, the correlations between a combination of predictor assessments (GMs at 1 and 3 months and WMA/GMs at 1 and 3 months) were also assessed with Spearman's rank correlation coefficient.

Sensitivity, specificity, positive and negative predictive values, and accuracy with 95% confidence intervals (CIs) were calculated for WMA and GMs at 1 and 3 months for predicting AIMS (normal versus suspicious/abnormal) and NSMDA (normal to minimal versus mild to severe) classifications of motor disability, as well as a diagnosis of cerebral palsy, at 12 months. To assess the predictive validity of the combination of predictor assessment (GMs at 1 and 3 months and WMA/GMs at 1 and 3 months), results were dichotomized as normal versus 1 or more abnormal results.

RESULTS

Eighty-six infants were recruited, representing 72% of eligible infants admitted to the unit during the recruitment period. Details of the included and excluded infants were previously published.[15] The perinatal characteristics of the study sample are described in Table 1. Of the 86 infants recruited, all infants underwent MRI and 12-month assessments. One infant did not have a GMs assessment at 1 month, because she was in a hip spica, and another infant was not seen at 3 months because her mother had returned to work, resulting in 84 (98%) infants having all assessments. The mean gestational age of the infants recruited was 27.3 (SD: 1.5) weeks, and mean birth weight was 1014 (SD: 265) g. Of the 86 infants, 42 (49%) were male, 20 (23%) were from multiple births, 6 (7%) had grade III/IV intraventricular hemorrhage, and 3 (3%) had PVL.

There were 76 (88%) infants who had no or mild WMA, and 10 (12%) infants who had moderate-to-severe WMA (Table 2). At 1 month, 53 (61%) infants were classified as having abnormal GMs, whereas at 3 months only 20 (23%) infants were classified as having

TABLE 1 Characteristics of the Study Sample ($N = 86$)

Characteristics	*n*	%
Gender, male	42	49
Birth weight <1000 g	44	51
Small for gestational age (−2SD)	7	8
Gestational age <28 weeks	48	56
IVH Grade III/IV	6	7
Cystic PVL (ultrasound)	3	3
Oxygen at 36 wk	27	31
Postnatal steroids	4	5
Proven or suspected necrotizing enterocolitis	15	17

TABLE 2 WMA and GMs Assessment Findings

Classification	*n* (%)
WMA ($n = 86$)	
Nil	22 (26)
Mild	54 (63)
Moderate	6 (7)
Severe	4 (5)
GMs at 1 mo ($n = 85$)	
Normal	32 (38)
PR	46 (54)
CS	7 (8)
Chaotic	0 (0)
GMs at 3mo ($n = 85$)	
Normal	65 (76)
Abnormal	0 (0)
Absent	20 (24)
GMs trajectory ($n = 84$)	
Consistently normal	32 (38)
PR and normal	33 (39)
PR and absent	12 (14)
CS and absent	7 (9)
WMA and GMs ($n = 84$)	
Consistently normal	32 (38)
1 abnormal assessment	32 (38)
2 abnormal assessments	11 (13)
3 abnormal assessments	9 (10)
AIMS ($n = 86$)	
Normal	56 (65)
Suspicious/abnormal	30 (35)
NSMDA ($n = 86$)	
Normal	47 (55)
Minimal	23 (27)
Mild	11 (13)
Moderate	4 (4)
Severe	1 (1)

n indicates number of infants; PR, poor repertoire; CS, cramped synchronized.

TABLE 3 Correlation Between Initial Assessments and Abnormal Motor Outcome at 12 Months' Corrected Age

Initial Assessment	Outcome Assessment	Spearman's *r*	*P*
WMA	AIMS	0.27	.012
	NSMDA	0.50	<.001
	CP	0.68	<.001
GMs at 1 mo	AIMS	0.31	.004
	NSMDA	0.24	.029
	CP	0.20	.072
GMs at 3 mo	AIMS	0.27	.015
	NSMDA	0.42	<.001
	CP	0.47	<.001
GMs trajectory	AIMS	0.34	.001
	NSMDA	0.37	<.001
	CP	0.40	<.001
WMA and GMs	AIMS	0.35	.001
	NSMDA	0.39	<.001
	CP	0.41	<.001

abnormal GMs (absent fidgety movements). Thirty-two (38%) infants had consistently normal GMs trajectory, 33 (39%) had a transient abnormal assessment, and 19 (23%) infants had a consistently abnormal trajectory. At 12 months, 30 (35%) infants were classified as having suspicious/abnormal development with the AIMS and 16 (18%) as having mild-to-severe motor dysfunction on the NSMDA. There were 5 (6%) infants classified as having CP at 12 months.

There was a significant relationship with all predictor assessments (WMA and GMs) and motor development at 12 months assessed with both the AIMS and NSMDA (Table 3). The strongest correlation between assessments was with WMA at term-equivalent age and NSMDA classification at 12 months. The combination of WMA and GMs assessments demonstrated the strongest correlation with AIMS classification at 12 months.

The sensitivity, specificity, positive, and negative predictive values and accuracy of the 3 predictor assessments are described in Table 4, with Table 5 describing the same results excluding infants with CP. The sensitivity and specificity of GMs trajectory and GMs in combination with WMA was the same as for GMs at 1 month, because all infants with moderate-to-severe WMA and abnormal GMs at 3 months had abnormal GMs at 1 month. All assessments had 100% sensitivity in detecting cerebral palsy; however, the sensitivity in detecting motor dysfunction on the NSMDA and AIMS was relatively poor for WMA and GMs at 3 months' corrected age. GMs at 1 month corrected age had the greatest sensitivity in detecting motor dysfunction on the NSMDA (86%) and suspicious/abnormal AIMS classification (83%); however, the specificity was low compared with the other assessments. Overall, WMA had the greatest combination of positive and negative predicting values, resulting in the greatest accuracy for predicting outcome at 12 months' corrected age. When the infants with CP are excluded from the analysis (Table 5), the sensitivity of WMA and GMs at 3 months' corrected age is reduced; however, the specificity of all 3 assessments is relatively similar.

DISCUSSION

This study demonstrated that both WMA assessed by MRI at term and GMs assessments at 1 and 3 months' corrected age are significantly associated with motor function at 12 months' corrected age for infants born very preterm. However, all assessments have some limitations in predicting motor development at 12 months' corrected age, with no test having 100% accuracy. WMA had the greatest specificity (94%–96%) of all assessments, and although the sensitivity of WMA was excellent for detecting cerebral palsy, the sensitivity for detecting motor dysfunction other than cerebral palsy was low. GMs at 1 month had excellent sensitivity in detecting motor dysfunction at 12 months' corrected age; however, this resulted in a large number of infants having false-positive results. GMs at 3 months had better specificity for predicting cerebral palsy, and hence a lower false-positive rate; however, the sensitivity was lower in a similar fashion to MRI.

Previous studies have reported that WMA correlates with later adverse motor outcome, including cerebral palsy.[7] However, this study is the first to our knowledge to examine the sensitivity and specificity in predicting motor dysfunction at 12 months' corrected age. The current study demonstrated that although moderate-to-severe WMA is highly predictive of cerebral palsy, it is not as useful in predicting other types of early motor dysfunction. This was demonstrated by the poor sensitivity of WMA to predict AIMS and NSMDA classifications when infants with cerebral palsy were excluded

TABLE 4 Sensitivity and Specificity of WMA and GMs in Predicting Abnormal Motor Development at 12 Months' Corrected Age

Initial Assessment	Outcome Assessment	Sensitivity (95% CI)	Specificity (95% CI)	Positive PV (95% CI)	Negative PV (95% CI)	Accuracy (95% CI)	χ^2	*P*
WMA	AIMS	23.3 (8.2–38.5)	94.6 (88.7–100.0)	70.0 (41.6–98.4)	69.7 (59.4–80.1)	69.8 (60.7–79.5)	6.14	.013
	NSMDA	43.8 (19.4–68.1)	95.7 (90.06–100.00)	70.0 (41.6–98.4)	88.2 (80.9–95.4)	86.5 (78.7–93.4)	19.74	<.001
	Cerebral palsy	100.0 (46.7–100.0)	93.8 (88.6–99.1)	50.0 (19.0–80.9)	100.0 (46.7–100.0)	94.0 (89.3–99.1)	40.35	<.001
GMs at 1 mo	AIMS	82.8 (69.0–96.5)	48.2 (35.1–61.3)	45.3 (31.9–58.7)	84.4 (71.8–97.0)	60.0 (49.6–70.4)	7.81	.005
	NSMDA	86.7 (96.5–100.0)	42.9 (31.3–54.5)	24.5 (12.9–36.1)	93.8 (85.36–100.00)	50.6 (40.0–61.2)	4.59	.032
	Cerebral palsy	100.0 (46.7–100.0)	40.0 (29.3–50.7)	9.4 (1.6–17.3)	100.0 (46.7–100.0)	43.5 (33.0–54.1)	3.21	.073
GMs at 3 mo	AIMS	40.0 (22.8–57.5)	85.5 (76.1–94.8)	60.0 (38.5–81.5)	72.3 (61.4–83.2)	69.4 (59.6–79.2)	6.99	.008
	NSMDA	62.5 (38.8–86.2)	85.5 (77.2–93.8)	50.0 (28.1–71.9)	90.8 (83.7–97.8)	81.2 (72.9–89.5)	16.64	<.001
	Cerebral palsy	100.0 (46.7–100.0)	81.3 (72.7–89.8)	0.3 (6.0–44.0)	100.0 (46.7–100.0)	82.4 (74.3–90.45)	12.26	<.001

PV indicates predictive value.

TABLE 5 Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value, and Accuracy in Predicting Abnormal Motor Outcome at 12 Months' Corrected Age Excluding Infants With Cerebral Palsy

Initial Assessment	Outcome Assessment	Sensitivity (95% CI)	Specificity (95% CI)	Positive PV (95% CI)	Negative PV (95% CI)	Accuracy (95% CI)	χ^2	*P*
WMA	AIMS	8.0 (0.0–18.6)	94.6 (88.7–100.0)	40.0 (0.0–82.9)	69.7 (59.4–80.1)	67.9 (57.7–78.1)	0.21	.648
	NSMDA	18.2 (0.0–41.0)	95.7 (90.1–100.0)	40.0 (90.0–82.9)	88.2 (80.9–95.4)	85.2 (77.5–92.9)	3.17	.075
GMs at 1m	AIMS	79.2 (62.9–95.4)	48.2 (35.1–61.3)	39.6 (25.1–61.3)	84.4 (71.8–97.0)	57.5 (46.7–68.3)	5.23	.022
	NSMDA	80.0 (55.2–100.0)	42.9 (31.3–54.5)	16.7 (6.1–27.2)	93.8 (85.4–100.0)	47.5 (36.6–58.4)	1.90	.168
GMs at 3 mo	AIMS	28.0 (10.4–45.6)	85.5 (76.1–94.8)	46.7 (21.4–71.9)	72.3 (61.4–83.2)	67.5 (57.2–77.7)	2.04	.153
	NSMDA	45.5 (16.0–74.9)	85.5 (77.2–93.8)	33.3 (9.5–57.2)	90.8 (83.7–97.8)	76.3 (66.9–85.6)	6.09	.015

PV indicates predictive value.

from the analysis. GMs during the fidgety age (46–60 weeks' postmenstrual age) were also reported to have excellent sensitivity and specificity in predicting cerebral palsy, whereas the predictive value of GMs during the writhing age (36 weeks' postmenstrual age to 7 weeks postterm) is reported to be lower.[13,25] The high frequency of poor repertoire GMs during the writhing period followed by normal GMs during the fidgety stage may explain the poor predictive value. Although the pathology that results in poor repertoire GMs is not fully understood, they have been shown to correlate with milder brain abnormalities (eg, minor or transient cranial ultrasound abnormalities and mild WMA on MRI) more than other forms of abnormal GMs.[15,18] Our finding that abnormal GMs at 1 month are associated with abnormal motor development, although with lower specificity than 3 months, does support the hypothesis that abnormal GMs during the writhing period may be associated with milder structural and functional abnormalities.

The rates of cerebral palsy vary in the literature from 7% to 18% for very preterm infants,[26] with the rate in the current study being 6%. However, 12 months is still relatively early in life to confirm the diagnosis of cerebral palsy because the difficulty in assessing tone and thus the rate may increase when the infants are assessed at older ages. The infants who were classified as having cerebral palsy in this study at 12 months are likely to have substantial motor problems, whereas there may be some infants who later are diagnosed with cerebral palsy who have relatively mild motor impairments that are not apparent at this early age. Furthermore, development occurs continuously, influenced by environmental, social, and biological factors, which makes it difficult to classify a child's motor development as normal or abnormal from a single examination. The plasticity of the brain in the early years of life, along with the influence of other factors on development, such as early intervention programs and maternal socioeconomic status, makes it unrealistic to expect an assessment in the early months of life will have 100% accuracy in predicting later outcome.

Given these limitations in predicting later motor development, WMA and GMs still have a role in the early assessment of the very preterm infants development as both assessments improve understanding of the potential developmental course. The findings in our study relating to the sensitivity and specificity are of value to the clinician in choosing and using these tools for evaluation of risk of adverse motor outcome. If the clinician is to prefer to have greater sensitivity, so that as many infants with potential developmental problems can be enrolled in early intervention as soon as possible to take advantage of the plasticity of the brain during the early years, then they may rely of GMs at 1 month. In contrast, for greater specificity, so as not to concern parents that their infant may have a motor problem and to wait to assess the infant's progress, then the MRI scan at term and GMs at 3 months would be more appropriate tools. MRI has the greatest accuracy in predicting motor dysfunction at 12 months' corrected age.

CONCLUSIONS

WMAs at term and early motor function assessed with Prechtl's GMs assessment both correlate with motor development at 12 months' corrected age for very preterm infants. Although WMA on MRI at term may have the greatest accuracy, it may not be easily accessible to some very preterm infants. GMs also seem to have a valuable role in prediction. Although GMs at 3 months' corrected age have greater accuracy than GMs at 1 month corrected age, it is recommended that both assessments are used. GMs at 1 month corrected age have the greatest sensitivity of all assessments for predicting cerebral palsy or other motor dysfunction. It is important to note that no test has 100% accuracy because of the influence of social, environmental, and biological factors on development.

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