General Movements in Very Preterm Children and Neurodevelopment at 2 and 4 Years

WHAT’S KNOWN ON THIS SUBJECT: Assessment of general movements (GM) in early infancy is predictive of adverse neurologic outcome, particularly cerebral palsy. There is limited evidence of the predictive value of GM for other domains of neurodevelopment such as language and cognitive impairment.

WHAT THIS STUDY ADDS: Abnormal GM in preterm infants in the first 3 months postterm are predictive of a range of neurodevelopmental outcomes in early childhood. GM at 3 months are more accurate at distinguishing later neurodevelopment impairment than those at 1 month.

abstract

OBJECTIVE: Although ~50% of very preterm (VP) children have neurodevelopmental impairments, early prediction of infants who will experience problems later in life remains a challenge. This study evaluated the predictive value of general movements (GM; spontaneous and endogenous movements) at 1 and 3 months’ corrected age for neurodevelopment at 2 and 4 years of age in VP children.

METHODS: At 1 and 3 months’ corrected age, infants born <30 weeks’ gestation had GM assessed as normal or abnormal. Motor, cognitive, and language development at 2 years was assessed by using the Bayley Scales of Infant and Toddler Development, Third Edition. At 4 years, cognitive and language outcomes were assessed by using the Differential Ability Scale–Second Edition and motor outcomes with the Movement Assessment Battery for Children–Second Edition; a diagnosis of cerebral palsy was documented.

RESULTS: Ninety-nine VP infants were recruited, with 97% and 88% of survivors followed up at age 2 and 4 years, respectively. Abnormal GM at 1 month were associated with worse motor outcomes at 2 and 4 years but not language or cognitive outcomes. Abnormal GM at 3 months were associated with worse motor, cognitive, and language outcomes at both 2 and 4 years. Overall, GM at 1 month demonstrated better sensitivity to impairments at 2 and 4 years, whereas GM at 3 months had better specificity and were more accurate overall at distinguishing between children with and without impairment.

CONCLUSIONS: Abnormal GM in VP infants, particularly at 3 months postterm, are predictive of worse neurodevelopment at ages 2 and 4 years. Pediatrics 2013;132:e452–e458

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KEY WORDS: general movements assessment, neurodevelopmental outcome, preterm infant

ABBREVIATIONS
Bayley-III—Bayley Scales of Infant and Toddler Development, Third Edition
CP—cerebral palsy
GM—general movements
MABC-2—Movement Assessment Battery for Children–Second Edition
MDI—Mental Developmental Index
PDI—Psychomotor Index
VP—very preterm

Dr Spittle coordinated data collection for the general movements assessment, carried out the initial analyses, and drafted and revised the manuscript; Dr Spencer-Smith coordinated data collection for the Movement Assessment Battery for Children–Second Edition and the Differential Ability Scale–Second Edition, and critically reviewed and revised the manuscript; Dr Cheong was involved in study design and critically reviewed the manuscript; Dr Eeles assisted in the data collection of the Bayley Scales of Infant and Toddler Development, Third Edition; Dr Lee oversaw the statistical analysis and critically reviewed the manuscript; Dr Anderson was involved in study design and reviewed and revised the manuscript; Dr Doyle was involved in the study design, supervised data collection, and critically reviewed the manuscript; and all authors approved the final manuscript as submitted.

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(Continued on last page)
Children born very preterm (VP, \(<30\) weeks’ gestation) are at risk for long-term neurodevelopmental problems, with almost one-half having motor, cognitive, and/or language impairments, a rate much higher than their term peers. Early identification of infants at risk for long-term impairments remains a challenge. A recent systematic review of randomized controlled trials of early-intervention programs for preterm infants found that motor and cognitive outcomes can be improved by intervening early, and animal studies emphasize that the environment can enhance or alter brain development.

General movements (GM) are part of an infant’s spontaneous movement repertoire. Observation of movement patterns in preterm and term infants from birth up to 20 weeks postterm age predicts later cerebral palsy (CP) and minor neurologic dysfunction. GM assessment differs in theoretical content from other motor assessments because it involves observation of the infant’s spontaneous movements, which are believed to be endogenously generated without being constantly triggered with specific sensory input. We have previously demonstrated that GM and white matter abnormality on MRI are predictive of motor development at 12 months’ corrected age in VP children. Although MRIs may require transportation of infants to a specialist facility, GM assessment is more feasible because it is done at the bedside.

Two recent systematic reviews of GM and their predictive validity called for more rigorous studies with long-term follow-up because of the many sources of bias in studies to date (eg, the assessors being familiar with the infant’s clinical history). The majority of studies have focused on prediction of CP and motor impairment, although some studies have demonstrated that GM are related to other areas of development, such as cognitive and behavioral outcomes. The goal of the current study was to assess the validity of GM assessments at 1 and 3 months’ corrected age for predicting a range of neurodevelopmental outcomes at 2 and 4 years’ corrected age in VP children. A strong association between GM at both times and motor, cognitive, and language development was hypothesized, with the strongest associations expected with motor impairment.

**METHODS**

**Participants**

Ninety-nine infants born \(<30\) weeks’ gestation between January 2005 and September 2006 and cared for at the Royal Women’s Hospital, Melbourne, Victoria, Australia, were studied. Children were included if they lived within 100 km of the hospital and at least 1 parent spoke English; they were excluded if they had a congenital abnormality known to affect development. The study cohort participated in a randomized controlled trial of a preventive care program. Because there was little evidence for differences in motor and cognitive performance between children in the intervention and control groups at 2 or 4 years’ corrected age, both groups were combined for the current study. The study was approved by the Royal Women’s Hospital and Royal Children’s Hospital human research ethics committees. Parents gave written informed consent for their child to participate.

**Procedure for GM Assessment at 1 and 3 Months**

Video recordings (20–30 minutes) of GM were obtained at 1 and 3 months’ corrected age. Recordings were scored by a certified pediatric physiotherapist (A.I.S.) blinded to clinical history, with reliability previously reported. The infants were videotaped lying supine during periods of alert wakefulness, wearing minimal clothing.

There are 2 distinct forms of GM: writhing and fidgety. At 1 month \((\pm 1\) week) corrected age, writhing GM were described as normal or abnormal.

- **Normal writhing movements**: a movement sequence of the whole body, with variation in arm, leg, neck, and trunk movements, which are characterized by their complexity, variability, and fluency.
- **Abnormal GM** are defined as:
  - Poor repertoire: monotonous movements, in which movements of body parts do not occur in the complex way seen in normal GM.
  - Cramped synchronized: muscles contract and relax almost simultaneously, resulting in the movements being rigid and lacking the smooth and fluent character of normal GM.
  - Chaotic: large amplitude movements of all limbs that occur chaotically, without fluency or smoothness.

At 3 months \((\pm 1\) week) corrected age, GM of a fidgety nature were described as normal or abnormal (“abnormal” or absent) according to the following descriptions:

- **Normal**: small movements of moderate speed and variable acceleration of neck, trunk, and limbs in all directions that are continual in the awake infant except during fussing and crying.
- **Abnormal**: larger amplitude movements than normal fidgety movements, with moderately exaggerated speed and jerkiness.
- **Absent**: fidgety movements are not observed.

Writhing GM were assessed at 1 month’s corrected age due to greater sensitivity and specificity than assessment at term age in preterm infants. Fidgety movements were assessed at 3 months’ corrected age because these movements are believed to peak at this age.
Assessments at 2 and 4 years’ corrected age were conducted by trained assessors with no knowledge of the child’s perinatal history and previous assessment results.

**Bayley Scales of Infant and Toddler Development, Third Edition**

At 2 years, motor, language, and cognitive outcomes were assessed by using the Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III). The motor, language, and cognitive composite scores have a mean ± SD of 100 ± 15. Although the Bayley-III is accepted as a valid and reliable measure of an infant’s neurodevelopment from 1 to 42 months, several studies have reported that it potentially underestimates impairments when using the published norms, and the use of a local reference group is preferable. Therefore, we used a local reference group that had been recruited in Victoria in 2005 as part of an ongoing longitudinal study. The group included 210 children born 37 to 42 weeks’ gestational age with no congenital abnormalities who were assessed at 2 years of age to determine impairment. Based on local data, scores >2 SDs below the reference group mean for motor (mean: 118.4 ± 16.7), cognitive (mean: 108.9 ± 14.3), and language (mean: 108.2 ± 14.8) composites were used to define moderate to severe impairment at 2 years.

**Cerebral Palsy**

At both 2 and 4 years, a diagnosis of CP was made by the child’s pediatrician and confirmed by the assessing physiotherapist, who was also blinded to clinical history. The Gross Motor Function Classification System was used to classify motor function further for all children, including those with CP. All children who were diagnosed as having CP at 2 years also had CP at 4 years. There were no new cases of CP at 4 years.

**Movement Assessment Battery for Children–Second Edition**

The Movement Assessment Battery for Children–Second Edition (MABC-2) is a valid and reliable tool for assessing motor performance in VP children and was used to identify children with motor impairments at 4 years. It produces an overall standard score (range: 1–19) and percentile rank based on norms from the United Kingdom. Total motor scores less than the fifth percentile were used to classify the child as having a moderate to severe motor impairment. Children too impaired to complete the MABC-2 were assigned a percentile of 1.

**Differential Ability Scale–Second Edition**

The Differential Ability Scale–Second Edition (DAS-II) was used to assess general cognitive functioning at 4 years. The general conceptual ability score provides a measure of general reasoning and conceptual abilities. The verbal composite score provides a measure of acquired verbal concepts and knowledge, and the nonverbal reasoning composite score gives a measure of complex, nonverbal, inductive reasoning requiring mental processing. Each scale has a standardized score (mean ± SD: 100 ± 15). Impairment was determined according to a local reference group, which comprised forty 4-year-old children recruited from local preschools, selected from suburbs of socioeconomic status similar to the suburbs of residence for the VP group at age 4 years based on the Socioeconomic Indexes for Areas (ie, the Index of Relative Disadvantage). Reference children were excluded if they had a birth weight <2500 g, had a documented history of a brain lesion or neurologic disability, or spoke no English. Based on these local normative data, scores >2 SDs below the mean for general conceptual ability (mean ± SD: 110.7 ± 10.8), verbal reasoning (mean: 106.4 ± 9.8), and nonverbal reasoning (mean: 108.6 ± 10.2) composites were used to classify the children as having a moderate to severe delay.

**Statistical Analysis**

Data were analyzed by using Stata version 12 (StataCorp, College Station, TX). Associations between GM (normal versus abnormal) at 1 and 3 months and continuous outcomes at 2 and 4 years were assessed by using linear regression. Models were fitted by using generalizing estimating equations to account for clustering of twins. However, due to convergence issues, sandwich estimators of variance were used to account for clustering with the language composite of the Bayley-III and nonverbal reasoning for the DAS-II. Sensitivity, specificity, and positive and negative predictive values, as well as accuracy (number correctly identified) and their 95% confidence intervals, were calculated for GM at 1 and 3 months for predicting moderate to severe impairment at 2 and 4 years.

**RESULTS**

Ninety-nine children had at least 1 GM assessment at 1 or 3 months’ corrected age (Fig 1). At 2 years, 97% (n = 94) of surviving children were assessed with the Bayley-III. Four children had missing language composite scores at 2 years because they did not speak English at home. At 4 years, 88% (n = 85) of surviving children attended the 4-year follow-up visit. Characteristics of the sample are presented in Table 1. At 1 month, 61% of children had abnormal GM (poor repertoire: n = 51 [53%]; cramped synchronized: n = 8 [8%]) (Table 2). By 3 months, 22% had abnormal GM (absent: n = 21 [22%]). The rates of moderate to severe...
neurodevelopmental impairments across all domains ranged from 11% to 13% at 2 years. At 4 years, the rate of moderate to severe impairment ranged from 15% to 23% across domains. The same 5 children had a diagnosis of CP at both 2 and 4 years (2 quadriplegia, 2 diplegia, 1 hemiplegia; 3 Gross Motor Function Classification System level II, 1 level III, and 1 level IV). None of the children with CP were able to complete the MABC-2.

Children with abnormal GM at 1 month had lower scores for all areas of neurodevelopment at 2 and 4 years (Table 3), but the only significant relationships were with the Bayley-II motor composite at 2 years and the MABC-2 standard scores at 4 years. There was strong evidence of an association between abnormal GM at 3 months and poorer outcomes across all domains at both time points, with the magnitude of some differences approaching 1 SD.

Predictive Validity of GM for Motor Impairment

GM at 1 month had excellent sensitivity (100%) for predicting moderate to severe motor impairment at 2 years or CP at either age but less sensitivity for moderate to severe impairment (73%) at 4 years (Table 4). However, specificity for GM at 1 month was poor for moderate to severe motor impairments at 2 and 4 years and CP at either age (42%–46%). The overall accuracy of GM at 1 month for predicting a future motor impairment (including CP) ranged from 45% to 51%.

GM at 3 months had 100% sensitivity for predicting CP; however, the sensitivity for predicting moderate to severe motor impairment was 70% at 2 years and 50% at 4 years. GM at 3 months had moderate sensitivity for predicting moderate to severe cognitive impairment at 2 years (70%) but poor sensitivity at 4 years (42%), although the specificity was good at both 2 (85%) and 4 (88%) years. The accuracy for GM at 3 months for predicting moderate to severe cognitive impairment was good at 83% and 77% for 2 and 4 years, respectively.

GM at 1 month had fair sensitivity for predicting moderate to severe language impairment at 2 years (73%), but the specificity was poor (39%). The sensitivity and specificity of GM at 1 month for predicting moderate to severe impairments in verbal and nonverbal reasoning at 4 years were generally low; the exception was sensitivity for moderate to severe nonverbal reasoning impairments (83%). Overall, the accuracy for GM at 1 month for predicting moderate to severe impairment in language at 2 years or verbal or nonverbal reasoning at 4 years ranged from 43% to 56%. GM at 3 months had low sensitivity for predicting moderate to severe impairment in language at 2 years or verbal or nonverbal reasoning at 4 years ranging from 43% to 58%, although the specificity was better (83%–87%). The accuracy for GM at 3 months for predicting moderate to severe impairment in language at 2 years or verbal or nonverbal reasoning at 4 years was good (74%–80%).

Predictive Validity of GM for Cognitive and Language Impairment

GM at 1 month had good sensitivity for predicting moderate to severe cognitive impairment at 2 (80%) and 4 (89%) years, although specificity was low (41%–48%) (Table 5). The accuracy of GM at 1 month for predicting moderate to severe cognitive impairment at 2 (46%) and 4 (57%) years was low. GM at 3 months had moderate sensitivity for predicting moderate to severe cognitive impairment at 2 years (70%) but poor sensitivity at 4 years (42%), although the specificity was good at both 2 (85%) and 4 (88%) years. The accuracy for GM at 3 months for predicting moderate to severe cognitive impairment was good at 83% and 77% for 2 and 4 years, respectively.

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**TABLE 1** Characteristics of the Study Sample

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N = 99</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight, g</td>
<td>1008 ± 265</td>
</tr>
<tr>
<td>Gestational age, wk</td>
<td>27.3 ± 1.5</td>
</tr>
<tr>
<td>Birth weight &lt;1000 g</td>
<td>51 (52)</td>
</tr>
<tr>
<td>Gestational age &lt;28 wk</td>
<td>55 (56)</td>
</tr>
<tr>
<td>Male</td>
<td>50 (51)</td>
</tr>
<tr>
<td>IVH grade III/IV</td>
<td>8 (8)</td>
</tr>
<tr>
<td>Cystic PVL (ultrasound)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Oxygen at 36 wk</td>
<td>36 (36)</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD or n (%). IVH, intraventricular hemorrhage; PVL, periventricular leukomalacia.

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FIGURE 1
Flowchart of recruitment and outcome assessments. *Not seen at 1 month but included at all other time points.
DISCUSSION

The current study demonstrated a strong association between GM at 1 and 3 months of age and subsequent motor outcomes at 2 and 4 years of age, consistent with the research of others and with our previous study examining the predictive validity of GM at 1 and 3 months for predicting motor development at 12 months. However, the relationship with GM and language and cognitive development is variable, with evidence of an association between abnormal GM at 3 months and lower scores on standardized measures of cognitive and language development at 2 and 4 years but not for GM at 1 month. Given that there is a marked difference in the associations with GM at the 2 different time periods and 2- and 4-year outcomes along with the sensitivity and specificity for moderate to severe delay, our findings support the theory that GM during the period when writhing movements occur (up to 6–9 weeks postterm) may have a different neural mechanism to GM during the period when fidgety movements occur (up to 16–20 weeks postterm).

Our study found that, in general, the sensitivity of GM at 1 month was good for predicting moderate to severe neurodevelopmental outcomes at 2 and 4 years, but the specificity was poor. Whereas GM at 3 months had better specificity than GM at 1 month for predicting later outcome, the sensitivity was variable. Overall, the accuracy for GM at 3 months was good for predicting all areas of neurodevelopment at 2 and 4 years, particularly motor and cognitive development, in which the accuracy was ≥80%. In contrast, GM at 1 month had poor accuracy for all areas of neurodevelopment. A study of 26 preterm infants (23–36 weeks’ gestation) reported findings similar to our study when assessing the predictive validity of GM for mild delay. Kodric et al also reported that GM at term had excellent sensitivity for predicting mild delay on the Bayley Scales of Infant Development Mental Developmental Index (MDI; 100%) and Psychomotor Index (PDI; 86%) but even lower rates of specificity than our study. At 3 months, they reported improved specificity for both MDI and PDI; however, it was still relatively low for both (MDI: sensitivity 83%, specificity 55%; PDI: sensitivity 61%, specificity 46%). Susteric et al reported that GM at 3 months’ corrected age had better sensitivity than GM at term for predicting motor impairment on the MABC-2 (100% vs 86%), but the specificity was again very low (24% at 3 months and 21% at 1 month) in a cohort of 45 children <36 weeks’ gestation.

Strengths of our study include its large prospective study design and excellent retention rates. In addition, it assessed

TABLE 2 GM Assessments at 1 and 3 Months and Neurodevelopmental Outcomes at 2 and 4 Years

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Age Corrected</th>
<th>No. Assessed</th>
<th>Classification</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GM</td>
<td>1 mo</td>
<td>97</td>
<td>Abnormal</td>
<td>59 (61)</td>
</tr>
<tr>
<td></td>
<td>3 mo</td>
<td>97</td>
<td>Domain</td>
<td>21 (22)</td>
</tr>
<tr>
<td>Bayley-III</td>
<td>2 y</td>
<td>94</td>
<td>Motor</td>
<td>10 (11)</td>
</tr>
<tr>
<td></td>
<td>94</td>
<td>Cognitive</td>
<td>10 (11)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>90</td>
<td>Language</td>
<td>12 (13)</td>
<td></td>
</tr>
<tr>
<td>CP</td>
<td>94</td>
<td></td>
<td></td>
<td>5 (5)</td>
</tr>
<tr>
<td>DAS-II</td>
<td>4 y</td>
<td>84</td>
<td>General cognitive</td>
<td>19 (23)</td>
</tr>
<tr>
<td></td>
<td>85</td>
<td>Verbal reasoning</td>
<td>13 (15)</td>
<td></td>
</tr>
<tr>
<td>MABC-2</td>
<td>82</td>
<td>Nonverbal reasoning</td>
<td>19 (23)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>76</td>
<td>Motor</td>
<td>16 (21)</td>
<td></td>
</tr>
<tr>
<td>CP</td>
<td>85</td>
<td></td>
<td></td>
<td>5 (6)</td>
</tr>
</tbody>
</table>

N: number of infants with data available.

* Moderate to severe impairment = scores <2 SDs below the normative mean on the Bayley-III or DAS-II or less than the fifth percentile on the MABC-2.

TABLE 3 Associations Between Abnormal GM at 1 and 3 Months and Neurodevelopment at 2 and 4 Years

<table>
<thead>
<tr>
<th>GM</th>
<th>Age at Follow-up</th>
<th>Outcome Assessment</th>
<th>N</th>
<th>Abnormal GM: Mean ± SD</th>
<th>Normal GM: Mean ± SD</th>
<th>Mean Difference* (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mo</td>
<td>Motor</td>
<td>92</td>
<td>96.5 ± 16.8</td>
<td>105.5 ± 14.9</td>
<td>-7.8 (-14.6 to -1.05)</td>
<td>.024</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cognitive</td>
<td>92</td>
<td>96.5 ± 13.2</td>
<td>101.4 ± 11.7</td>
<td>-4.8 (-9.9 to 0.26)</td>
<td>.083</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Language</td>
<td>92</td>
<td>96.8 ± 15.8</td>
<td>102.8 ± 15.8</td>
<td>-6.1 (-12.0 to -0.1)</td>
<td>.079</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MABC–2 standard score</td>
<td>74</td>
<td>9.1 ± 5.6</td>
<td>9.4 ± 2.6</td>
<td>-0.3 (-7.7 to 7.1)</td>
<td>.937</td>
</tr>
<tr>
<td></td>
<td></td>
<td>General conceptual ability</td>
<td>82</td>
<td>95.6 ± 17.4</td>
<td>99.5 ± 11.8</td>
<td>-2.9 (-9.6 to 3.8)</td>
<td>.397</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Verbal reasoning</td>
<td>83</td>
<td>96.0 ± 17.7</td>
<td>96.3 ± 12.9</td>
<td>0.3 (-7.7 to 7.1)</td>
<td>.937</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nonverbal reasoning</td>
<td>80</td>
<td>97.1 ± 13.4</td>
<td>101.7 ± 11.1</td>
<td>-4.6 (-9.9 to 0.7)</td>
<td>.087</td>
</tr>
<tr>
<td></td>
<td>3 mo</td>
<td>Motor</td>
<td>94</td>
<td>87.8 ± 19.3</td>
<td>102.9 ± 14.2</td>
<td>-15.1 (-2.9 to -6.3)</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cognitive</td>
<td>94</td>
<td>92.0 ± 17.6</td>
<td>100.4 ± 10.8</td>
<td>-7.4 (-15.9 to -0.9)</td>
<td>.025</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Language</td>
<td>90</td>
<td>88.8 ± 19.3</td>
<td>101.4 ± 14.0</td>
<td>-11.6 (-20.0 to 3.1)</td>
<td>.008</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MABC–2 standard score</td>
<td>76</td>
<td>5.8 ± 4.1</td>
<td>9.2 ± 2.7</td>
<td>-3.4 (-5.5 to -1.5)</td>
<td>.002</td>
</tr>
<tr>
<td></td>
<td></td>
<td>General conceptual ability</td>
<td>84</td>
<td>85.5 ± 18.3</td>
<td>99.8 ± 13.4</td>
<td>-14.3 (-23.9 to -5.1)</td>
<td>.003</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Verbal reasoning</td>
<td>85</td>
<td>87.1 ± 21.1</td>
<td>98.7 ± 13.0</td>
<td>-11.6 (-21.8 to -1.4)</td>
<td>.026</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nonverbal reasoning</td>
<td>82</td>
<td>91.0 ± 11.0</td>
<td>100.4 ± 12.1</td>
<td>-9.3 (-15.0 to -3.6)</td>
<td>.001</td>
</tr>
</tbody>
</table>

Motor outcome at 4 years is measured as a standardized score (mean ± SD: 10 ± 3); all other outcomes are scale scores (mean: 100 ± 15). CI, confidence interval.

* Mean difference from linear regression where models were fitted by using generalizing estimating equations to account for clustering of twins.
TABLE 4 Sensitivity and Specificity of Abnormal GM at 1 and 3 Months of Age for Predicting Moderate to Severe Motor Impairment at 2 and 4 Years

<table>
<thead>
<tr>
<th>GM</th>
<th>Age at Follow-up</th>
<th>Outcome</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mo</td>
<td>2 y</td>
<td>Moderate to severe impairment (Bayley-III)</td>
<td>100 (63 to 100)</td>
<td>43 (33 to 55)</td>
<td>16 (8 to 29)</td>
<td>100 (88 to 100)</td>
<td>49 (38 to 59)</td>
</tr>
<tr>
<td></td>
<td>4 y</td>
<td>Moderate to severe impairment (MABC-2)</td>
<td>72 (45 to 91)</td>
<td>46 (33 to 59)</td>
<td>20 (14 to 41)</td>
<td>74 (59 to 86)</td>
<td>51 (40 to 62)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CP</td>
<td>100 (46 to 100)</td>
<td>42 (31 to 53)</td>
<td>10 (4 to 22)</td>
<td>100 (87 to 100)</td>
<td>45 (34 to 56)</td>
</tr>
<tr>
<td>3 mo</td>
<td>2 y</td>
<td>Moderate to severe impairment (Bayley-III)</td>
<td>70 (35 to 92)</td>
<td>85 (75 to 91)</td>
<td>35 (16 to 59)</td>
<td>96 (88 to 99)</td>
<td>83 (75 to 91)</td>
</tr>
<tr>
<td></td>
<td>4 y</td>
<td>Moderate to severe impairment (MABC-2)</td>
<td>50 (26 to 74)</td>
<td>88 (76 to 95)</td>
<td>53 (27 to 78)</td>
<td>87 (75 to 94)</td>
<td>80 (71 to 88)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CP</td>
<td>100 (46 to 100)</td>
<td>84 (74 to 91)</td>
<td>28 (11 to 54)</td>
<td>100 (93 to 100)</td>
<td>85 (77 to 93)</td>
</tr>
</tbody>
</table>

Moderate to severe impairment = scores < 2 SDs below the normative mean on the Bayley-III total motor composite, and less than the fifth percentile on MABC-2. CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

TABLE 5 Sensitivity and Specificity of GM at 1 and 3 Months of Age for Predicting Moderate to Severe Cognitive, Language, Verbal, or Nonverbal Impairment at 2 and 4 Years

<table>
<thead>
<tr>
<th>GM</th>
<th>Age at Follow-up</th>
<th>Outcome</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mo</td>
<td>2 y</td>
<td>Cognitive</td>
<td>80 (44 to 96)</td>
<td>41 (31 to 53)</td>
<td>14 (7 to 27)</td>
<td>94 (80 to 99)</td>
<td>46 (38 to 56)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Language</td>
<td>73 (39 to 83)</td>
<td>39 (28 to 51)</td>
<td>14 (7 to 27)</td>
<td>91 (74 to 98)</td>
<td>45 (35 to 53)</td>
</tr>
<tr>
<td></td>
<td>4 y</td>
<td>General cognitive ability</td>
<td>89 (64 to 98)</td>
<td>48 (36 to 61)</td>
<td>33 (20 to 48)</td>
<td>87 (52 to 80)</td>
<td>57 (46 to 68)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Verbal reasoning</td>
<td>62 (52 to 85)</td>
<td>40 (29 to 52)</td>
<td>16 (8 to 30)</td>
<td>85 (57 to 94)</td>
<td>43 (32 to 54)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nonverbal reasoning</td>
<td>83 (58 to 96)</td>
<td>48 (36 to 61)</td>
<td>32 (20 to 47)</td>
<td>91 (75 to 98)</td>
<td>56 (45 to 67)</td>
</tr>
<tr>
<td>3 mo</td>
<td>2 y</td>
<td>Cognitive</td>
<td>70 (35 to 92)</td>
<td>85 (75 to 91)</td>
<td>35 (16 to 59)</td>
<td>96 (88 to 99)</td>
<td>83 (75 to 91)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Language</td>
<td>58 (29 to 84)</td>
<td>80 (73 to 90)</td>
<td>35 (16 to 59)</td>
<td>93 (83 to 97)</td>
<td>80 (72 to 88)</td>
</tr>
<tr>
<td></td>
<td>4 y</td>
<td>General cognitive ability</td>
<td>42 (21 to 66)</td>
<td>88 (77 to 94)</td>
<td>50 (26 to 74)</td>
<td>84 (72 to 91)</td>
<td>77 (68 to 86)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Verbal reasoning</td>
<td>54 (26 to 80)</td>
<td>85 (74 to 92)</td>
<td>39 (18 to 64)</td>
<td>91 (81 to 96)</td>
<td>80 (72 to 88)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nonverbal reasoning</td>
<td>32 (14 to 57)</td>
<td>87 (76 to 94)</td>
<td>43 (19 to 70)</td>
<td>81 (69 to 89)</td>
<td>74 (65 to 83)</td>
</tr>
</tbody>
</table>

Moderate to severe impairment = scores < 2 SDs for motor, cognitive, and language scales on the Bayley-III and general cognitive ability, verbal reasoning, and nonverbal reasoning on the DAS-II. CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

a wider range of neurodevelopmental outcomes than previous studies, including language at 2 years and verbal and nonverbal reasoning at 4 years. However, the study has some limitations. There are a variety of abnormal GM patterns that can be seen at 1 month, including poor repertoire and chaotic and cramped synchronized movements. Cramped synchronized movements have been shown to be more predictive than poor repertoire GM in predicting severe adverse neurologic outcome. However, we combined both movement patterns because we wanted to assess the predictive validity of abnormal GM rather than different patterns, and there were only a limited number of subjects with cramped synchronized movements. Further studies examining the predictive validity of different types of GM are warranted. Assessment of neurodevelopment at 2 and 4 years required different measurement tools because the same assessments were not available for both ages. Although the tools used are reported to be valid and reliable for assessing motor, cognitive, and language development, their constructs vary, which may explain some of the differences seen at 2 years versus 4 years. For example, the rate of children with moderate to severe motor impairment at 2 years was 11% as assessed on the Bayley-III motor scale compared with 21% as assessed on the MABC-2 at 4 years. The Bayley-III has been shown to underestimate neurodevelopmental impairments in preterm children. However, it is the gold standard measurement tool for 2 years of age and allows comparison with other studies.

Our results are consistent with the findings of the most recent systematic review of GM and prediction of outcome, which reports that GM are most strongly associated with CP and other forms of motor impairment. However, our study also found that abnormalities in VP infants’ movements in early development are associated with cognitive and language outcomes at 2 and 4 years. This finding is likely due to strong correlation between GM and white matter abnormality, although further research is required to validate this theory. Clinicians and researchers should be aware when assessing an infant’s GM that abnormal movements are not only associated with motor impairments but also difficulties in other areas of development that may require a range of early-intervention services and/or follow-up. Further research is needed to compare the predictive validity of GM and other clinical tools, such as MRI, that have also been shown to correlate with outcomes.

CONCLUSIONS

The quality of GM in the first 3 months postterm are predictive of a range of neurodevelopmental outcomes at 2 and 4 years of age in VP children. GM at 1 and 3 months demonstrate different patterns of sensitivity and specificity for motor, cognitive, and language outcomes, with the strongest associations seen with GM at 3 months.
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(Continued from first page)

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