The quality of the early motor repertoire in preterm infants is predictive for minor neurological dysfunction at school age

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Abstract

Objective: The quality of the spontaneous motor repertoire at 3 to 4 months post-term has a high predictive power for later cerebral palsy (CP). The predictive power of the quality of the motor repertoire at this early age for minor neurological dysfunction (MND) is, as yet, less clear. Our aim was to investigate the predictive value of the quality of the early motor repertoire for the development of MND at school age.

Study design: Video-recordings of the spontaneous motor repertoire were made between 6 and 24 weeks post-term in 82 preterm infants (gestational age 29.7±1.9 w, birth weight 1183±302 g) in this prospective cohort study. We assessed several qualitative aspects of the motor repertoire. At 7 to 11 years of age, Touwens' neurological examination was performed. Children were classified as neurologically normal, MND and CP.

Results: At 7 to 11 years of age, 15 children (18%) had CP, 49 (60%) were neurologically normal, and 18 (22%) had MND. Multiple logistic regression analysis showed that 2 items in the motor repertoire had independent prognostic value for MND at school age: the quality of FMs and the quality of the concurrent motor repertoire, both at particularly 11-16 weeks post-term. In 7 of 11 children (64%), abnormal FMs evolved into MND. Normal FMs were followed by MND in 10 of 49 children (20%) (p<0.05). When FMs were normal, the quality of the concurrent motor repertoire provided additional information. Nine of the 28 children (32%) with normal FMs and an abnormal concurrent motor repertoire developed abnormally (8 MND, 1 CP). Only one of 21 children (5%) with normal FMs and a normal concurrent motor repertoire developed abnormally (MND) (p<0.05).

Conclusions: The quality of the early motor repertoire, in particular an abnormal quality of FMs and an abnormal quality of the concurrent motor repertoire at 11-16 weeks post-term, is associated with the development of MND at 7 to 11 years of age. The absence of such abnormalities is associated with low risk for later neurological problems. Assessment of the quality of the early motor repertoire enables the accurate early identification of individual infants at high and low risk for later neurological problems.

Introduction

Neurological and developmental complications are common in infants born preterm. Estimates of their prevalence range from 10% to more than 50%. Well-documented sequelae of preterm birth that persist into childhood and adolescence include motor, cognitive and behavioral impairments ranging in severity from cerebral palsy (CP) and sensory loss to minor neurological dysfunction (MND), learning disabilities, and attention and behavior problems. The early identification of infants at highest risk remains difficult. Gestational age and birth weight are two rather rough early indicators. Neuro-imaging (brain ultrasound and MRI) and specific clinical risk scores are slightly more accurate. In the last 15 years, the quality of spontaneous general movements (GMs), assessed following Prechtl’s method, has emerged as a reliable and valid predictor of severe neurological deficits, e.g. CP, for the individual infant. This method is based on visual Gestalt perception of the quality of GMs in the preterm, term and post-term periods, up to 5 months post-term. Normal GMs are characterised by complexity, variability and fluency, whereas abnormal GMs are characterised by reduced complexity, variability and fluency. At 6 to 9 weeks post-term age, the character of the GMs gradually changes into so-called “fidgety” GMs (FMs). The quality of these FMs, which can be observed up to 20 weeks post-term, is a particularly accurate marker for neurological outcome: most infants (96%) with normal FMs have normal neurological outcomes, while most
The quality of the early motor repertoire in preterm infants

Infants (95%) in whom FMs are absent during this particular age period develop CP. An early indicator with comparable prognostic value for the milder deficits (e.g. MND), which are far more prevalent than CP in this population, has not yet been identified.

Previously, associations have been found between the development of MND in childhood and the quality of GMs at 2-4 months post-term. Groen et al showed that abnormal GMs at 8-17 weeks post-term were predictors for coordination problems and fine manipulative disability at school age. However, the predictive value of GMs in Groen et al’s study, in which movement quality was assessed globally, was only fair. They based the degree of abnormality of the GMs on the extent to which the complexity and variation of spontaneous movements were reduced. Further, the abnormality of FMs and in particular their absence, despite its high predictive value for CP, were not taken into account.

In an earlier study, we followed a different approach, carrying out separate global assessments of different qualitative aspects of the motor repertoire. We found that both an abnormal quality of FMs and a monotonous character of concurrent movements increased the probability of developing MND at 2 years of age. The question then arises whether the assessment of the quality of FMs, in conjunction with the assessment of the quality of the concurrent motor repertoire, also has predictive value for MND at school age. Since FMs emerge at 6 weeks and disappear around 20 weeks post-term, we investigated whether the quality of the motor repertoire at 6 to 24 weeks post-term has prognostic value for MND at the age of 7-11 years in preterm infants.

Methods

Subjects
The study group consisted of 82 infants (50 boys and 32 girls) born preterm between September 1992 and October 1997 and admitted to the Neonatal Intensive Care Unit (NICU) of the Beatrix Children’s Hospital of the University Medical Center of Groningen (UMCG). The infants were members of a larger group of 99 infants who were included in prospective studies of the prognostic value of the quality of GMs for neurological and developmental findings. The results of these studies have been reported previously. The study group can be considered a representative sample of the preterm infant population in our NICU (tertiary referral centre) during the mid-nineties.

Seven infants died during the first few months of life, mostly due to severe respiratory problems as seen in bronchopulmonary dysplasia. Conditions which could interfere with normal neurological development became apparent in three infants (two infants: blindness due to retinopathy of prematurity; one infant: morbus Duchenne). Five of the remaining 89 infants could not be traced. Two families refused to participate. Obstetrical and neonatal data are listed in table 1 grouped according to the neurological status at school age. All parents gave written, informed consent. The ethical review board of the UMCG approved the study.
Chapter 3

Recording and evaluation of the motor repertoire between 6 and 24 weeks post-term

Video recordings, approximately 10 minutes long, were made of the infants at approximately 6-8, 12-14 and 18-21 weeks during the post-term period. The timing and frequency of the video recordings differed for a few infants for logistic or family reasons. The recordings were made either at the outpatient clinic or at home, during periods of active wakefulness between feeds, with the partly dressed infants lying in supine position.

In toto, 214 recordings (median 3 per infant, mean duration 9:01 minutes) were available for analysis. The recordings of all infants were ordered according to increasing post-term age and evaluated offline by JLMB, AFB and CE according to Einspieler et al. Two of the observers were unaware of the infant’s clinical history and neurological status; one knew the infant’s clinical history. The quality

### Table 1. Clinical characteristics and risk factors of the study group, according to neurological findings at school age. Data are expressed as median (P25-75), or N (%).

<table>
<thead>
<tr>
<th></th>
<th>Children who developed normally or simple MND</th>
<th>Children who developed complex MND</th>
<th>Children who developed CP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>49</td>
<td>18</td>
<td>15</td>
</tr>
<tr>
<td>Gestational Age</td>
<td>30.1 wk (28.6 – 31.7 wk)</td>
<td>28.9 wk (27.8 – 31.0 wk)</td>
<td>28.7 wk (27.7-30.0 wk)</td>
</tr>
<tr>
<td>Birth Weight (BW)</td>
<td>1160 g (950 – 1343 g)</td>
<td>1165 g (898 – 1333 g)</td>
<td>1220 g (870-1460 g)</td>
</tr>
<tr>
<td>Male infants</td>
<td>23 (47)</td>
<td>12 (67)</td>
<td>12 (80)</td>
</tr>
<tr>
<td>IUGR (BW &lt; P5)</td>
<td>12 (24)</td>
<td>4 (22)</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Prenatal steroids</td>
<td>34 (71)</td>
<td>11 (61)</td>
<td>9 (60)</td>
</tr>
<tr>
<td>Apgar score at 5’</td>
<td>8 (8 – 9)</td>
<td>8 (5 – 8.3)</td>
<td>6 (5 – 7)</td>
</tr>
<tr>
<td>Umbilical pH</td>
<td>7.28 (7.25 – 7.31)</td>
<td>7.26 (7.21 – 7.33)</td>
<td>7.26 (7.21 – 7.33)</td>
</tr>
<tr>
<td>Ventilator support</td>
<td>(IPPV of HFOV)2</td>
<td>23 (47)</td>
<td>11 (61)</td>
</tr>
<tr>
<td>Septicaemia</td>
<td>17 (35)</td>
<td>7 (39)</td>
<td>5 (33)</td>
</tr>
<tr>
<td>ICH gr 1-2</td>
<td>11 (22)</td>
<td>6 (33)</td>
<td>2 (13)</td>
</tr>
<tr>
<td>ICH gr 3-4</td>
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<td>none</td>
<td>5 (33)</td>
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<tr>
<td>PVL1 gr1</td>
<td>19 (39)</td>
<td>14 (78)</td>
<td>8 (53)</td>
</tr>
<tr>
<td>PVL1 gr 2-3</td>
<td>none</td>
<td>none</td>
<td>4 (27)</td>
</tr>
<tr>
<td>BPD</td>
<td>11 (22)</td>
<td>5 (28)</td>
<td>9 (60)</td>
</tr>
<tr>
<td>Postnatal steroids</td>
<td>3 (6)</td>
<td>4 (22)</td>
<td>9 (60)</td>
</tr>
</tbody>
</table>

1 IUGR is intra-uterine growth restriction, birth weight according to the Dutch weight centiles of Kloosterman.
2 IPPV is intermittent positive pressure ventilation, HFOV is high frequency oscillatory ventilation.
3 ICH is intracranial haemorrhage graded according to Papile et al.
4 PVL is periventricular leukomalacia graded according to de Vries et al. PVL grade 1 is also called prolonged flaring.
5 BPD is Bronchopulmonary dysplasia, defined as oxygen dependency at 36 weeks postmenstrual age.

* P<0.05, compared with infants who developed normally or simple MND
* P<0.01, compared with infants who developed normally or simple MND
* P<0.05, compared with infants who developed complex MND
* P<0.01, compared with infants who developed complex MND

Recording and evaluation of the motor repertoire between 6 and 24 weeks post-term

Video recordings, approximately 10 minutes long, were made of the infants at approximately 6-8, 12-14 and 18-21 weeks during the post-term period. The timing and frequency of the video recordings differed for a few infants for logistic or family reasons. The recordings were made either at the outpatient clinic or at home, during periods of active wakefulness between feeds, with the partly dressed infants lying in supine position.

In toto, 214 recordings (median 3 per infant, mean duration 9:01 minutes) were available for analysis. The recordings of all infants were ordered according to increasing post-term age and evaluated offline by JLMB, AFB and CE according to Einspieler et al. Two of the observers were unaware of the infant’s clinical history and neurological status; one knew the infant’s clinical history. The quality
of the motor repertoire could not be judged in 10 of the 214 recordings (4.7%), due to crying, sleepiness or hiccups.

We assessed the quality of FMs and the quality of the concurrent motor repertoire separately during different runs of the videotapes. For further analysis, we clustered the video recordings between the ages of 6-10 weeks post-term (early fidgety movements’ period), 11-16 weeks (mid-fidgety movements’ period) 17-24 weeks (late or post-fidgety movements’ period). If two recordings were made of the same infant during the same age period, the recording closest to the median age of the particular age period was selected. We chose these periods (1) because of the age-related characteristics of the quality of FMs and (2) because, with time, the number of movement patterns, and therefore the complexity of the motor repertoire increases considerably.11,26,27

The quality of fidgety movements (FMs)

FMs are of small amplitude, moderate speed and variable acceleration of neck, trunk and limbs in all directions. They are continual in the awake infant, except during fussing and crying.13 FMs may be seen as early as 6 weeks post-term but usually appear around 9 weeks and persist until 15 to 20 weeks.11 We assessed the quality of FMs as normal, abnormal (amplitude, speed and jerkiness were exaggerated) or absence of FMs (no FMs observed between 6 and 20 weeks’ post-term). When FMs were present, their temporal organisation was scored as continual (++), intermittent (+) or sporadic (+/-)28 and their spatial organisation was scored as proximal (more prominent in the trunk, neck, shoulders and hips), distal (more prominent in the wrists and ankles), or equally prominent in the proximal and distal parts of the body.11

Quality of the concurrent motor repertoire

The quality of the concurrent motor repertoire was considered to be normal if it was smooth, variable, fluent and complex. Reduced complexity (monotony), jerkiness and/or stiffness were considered to be signs of abnormality, and were scored separately.17,21 Differences in degree of monotony, jerkiness and stiffness were not scored.

Inter-scorer reliability

To check inter-observer reliability, 145 randomly selected recordings were assessed by three observers. Cohen’s kappa was 0.87 for the quality of fidgety movements and 0.91 for the quality of the concurrent motor repertoire.

Assessment of neurological and motor findings at 7 to 11 years of age

Follow-up consisting of pediatric and neurological examinations was performed at regular intervals. At 6 years of age, 15 children were diagnosed with CP according to Hagberg’s criteria.29 A neurological examination according to Touwen30 was performed between 7 and 11 years of age on the remaining 67. This examination is designed to detect signs of minor neurological dysfunction.
Following Hadders-Algra, six subcategories of function were assessed posturing and muscle tone, reflexes, choreiform dyskinesia, coordination and balance, fine manipulative ability and rarely occurring dysfunctions, including an excess of associated movements. The children were classified as neurologically normal, simple MND, or complex MND. Simple MND denoted the presence of dysfunction in one or two subcategories, and complex MND the presence of dysfunction in more than two subcategories. Since simple MND has limited clinical and functional significance, as opposed to complex MND, the normal and simple-MND groups were analysed as a single group. Further, because the aim of the study was to evaluate the significance of the quality of the movement repertoire for minor neurological deficits, the analysis was performed both with and without the children with CP.

In addition, the Movement ABC, a test of motor skill for children in the age range 4 to 12 years, was administered. The Movement ABC, which is widely used in practice and in research, yields a score for total movement quality, based on separate scores for fine motor skills, ball skills and balance. The tasks which comprise the Movement ABC are representative of the motor skills that are required of children attending elementary school. They are adapted to the age of the child.

**Statistical analysis**

Statistical analysis was performed using SPSS package for Windows, version 14.0. Fisher’s exact test and Chi² test for trend were used to evaluate the associations between the categorical parameters of the quality of FMs and the concurrent motor repertoire on the one hand and neurological findings at school age on the other. The Kruskal-Wallis test and the Mann-Whitney U test were applied to evaluate the associations between clinical data and later neurological findings. To assess the influence of the different clinical and movement-quality-related factors on later neurological findings, backward multiple logistic regression analysis was performed. Only factors that were significant in the univariate analyses were included in the model. Throughout the analyses $p < 0.05$ (two-tailed tested) was considered to be statistically significant.

**Results**

**The neurological and movement ABC findings at school age**

At 7 to 11 years of age, 15 children had developed cerebral palsy (5 unilateral, 8 bilateral, 2 dyskinetic cerebral palsy). Of the remaining 67 children, 36 were neurologically normal, 13 had developed simple MND and 18 had complex MND. Most children with complex MND had abnormalities in the clusters coordination/ balance and fine manipulative ability. This combination of abnormal clusters was present in only 3 infants with simple MND.

All clusters of the neurological test except reflexes correlated significantly with the Movement ABC scores. The total score and all subtest scores on the Movement-ABC were similar for children classified...
The quality of the early motor repertoire in preterm infants

The total score and the subtest scores for fine motor and ball skills for children classified as simple and complex MND differed significantly (Mann Whitney U test, \( p = 0.002 \), \( p = 0.022 \) and \( p = 0.018 \) respectively). The difference in scores for balance almost reached statistical significance (\( p = 0.056 \)). These findings confirm the proposed differences in functional consequences between simple and complex MND and support the decision to combine the normal and simple MND groups for further analysis. For the purpose of clarity, this combined group is referred to as normal in this paper.

Relationship between clinical data at birth and neurological findings at school age

The associations between the peri- and neonatal clinical data and the neurological findings at school age are shown in Table 1. Several clinical data differed significantly between infants with CP and those who developed complex MND or were classified as normal. Hardly any differences in clinical data existed between infants who developed complex MND and infants who were classified as normal. Only a lower Apgar score at 5 minutes and the presence of prolonged flaring (periventricular leukomalacia grade 1) were more often seen in the MND infants.

Relationship between qualitative aspects of the motor repertoire and neurological findings at school age

a. Quality of fidgety movements between 6 and 24 weeks post-term

The associations between the quality of FMs and the neurological findings at school age for each age-period are shown in Table 2. The absence of FMs at 11-16 weeks post-term was most strongly

Table 2. Association between quality of GMs at post-term ages of 6-10 weeks, 11-16 weeks and 17-24 weeks and neurological findings at school age. The numbers in the boxes refer to the numbers of infants. For all age periods, these associations were highly significant (6-10wk post-term: Chi² test for trend = 28.5, \( p < 0.001 \); 11-16wk post-term: Chi² test for trend = 62.4, \( p < 0.001 \); 17-24 wk post-term: Chi² test for trend = 7.6, \( p = 0.011 \)).

<table>
<thead>
<tr>
<th>Post-term age</th>
<th>Quality of FMs</th>
<th>Neurological findings at school age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal FMs</td>
<td>Normal/ Simple MND</td>
</tr>
<tr>
<td>6-10 weeks</td>
<td>Normal FMs</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>Abnormal FMs</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Absence of FMs</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>34</td>
<td>15</td>
</tr>
<tr>
<td>11-16 weeks</td>
<td>Normal FMs</td>
<td>39</td>
</tr>
<tr>
<td></td>
<td>Abnormal FMs</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Absence of FMs</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>43</td>
<td>17</td>
</tr>
<tr>
<td>17-24 weeks</td>
<td>Normal FMs</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Abnormal FMs</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Absence of FMs</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>34</td>
<td>10</td>
</tr>
</tbody>
</table>
associated with adverse neurological outcome, preceding CP in 12 of 13 infants (92%), complex MND in one infant and never being observed in an infant later classified as normal. Absence of FMs at 6-10 weeks and at 17-24 weeks, however, was observed in several infants later classified as normal. In all of these infants, FMs were present at 11-16 weeks. In some infants they were normal. In others they were abnormal.

Abnormal FMs were observed most frequently at 11-16 weeks post-term. They preceded complex MND in 7 of 11 cases (64%). The remaining 4 infants (36%) were later classified as normal. Abnormal FMs were rare at both 6-10 weeks and 17-24 weeks. However, all but one of the infants who showed abnormal FMs at 11-16 weeks had either absent or abnormal FMs both before (6-10 weeks) and after (17-24 weeks) that period. Only one infant was inconsistent, showing normal FMs at 6-10 weeks.

At any age, approximately 80% of infants who showed normal FMs were classified as normal at school age. Normal FMs preceded CP in only one infant. Again, the association between the presence of normal FMs and normal neurological outcome was strongest at 11-16 weeks. However, normal FMs at 11-16 weeks preceded complex MND in 9 of 49 infants (18%).

Overall, the quality of FMs at 11-16 weeks had the strongest association with neurological outcome. However, while it differentiated the infants with complex MND from the infants with CP very well, it differentiated the infants with complex MND from the normal infants less clearly. Only half of the infants who developed complex MND (8 of 17 infants) had abnormal FMs at 11-16 weeks. The other half (9 of 17 infants) had normal FMs.

The groups did not differ on the detailed aspects of FMs, such as the temporal characteristics and proximal – distal predominance.

b. Quality of the concurrent motor repertoire between 6 and 24 weeks post-term

The associations between the quality of the concurrent motor repertoire in each age period and the neurological findings at school age are shown in Table 3. At all ages the concurrent motor repertoire was frequently abnormal, ranging from 68% to 72% of all infants. The association between the quality of the concurrent motor repertoire and neurological findings was strongest at 11-16 weeks post-term. A normal concurrent motor repertoire at this age distinguished the infants who were later classified as normal from those who developed either complex MND or CP (Figure 1a), preceding complex MND in only 1 of 21 infants (5%), and never preceding CP (Table 3). An abnormal concurrent motor repertoire, however, had less predictive value, preceding complex MND in 16 (31%), and CP in 13 of 52 infants (25%). Thus, nearly half of the infants (23 of 52, 44%) whose concurrent motor repertoire was abnormal at 11-16 weeks were later classified as normal.

Three types of concurrent motor repertoire abnormality were scored: monotony, jerkiness and stiffness. Of these, only monotony was associated with later complex MND (Figure 1b). The concurrent motor repertoire was monotonous in 80% of infants who later developed complex MND, as opposed to 30% of infants later classified as normal. Jerkiness and stiffness at any age did not differentiate between the two groups (Figure 1c-d).
The quality of the early motor repertoire in preterm infants

Table 3. Association between the quality of the concurrent motor repertoire at post-term ages of 6-10 weeks, 11-16 weeks and 17-24 weeks and neurological findings at school age. Signs of abnormality of the concurrent motor repertoire included a reduced complexity (monotony), jerkiness and / or stiffness. The numbers in the boxes refer to the number of infants. For all age periods, these associations were significant. (6-10wk post-term: \( \chi^2 \) test for trend = 12.0, \( p = 0.001 \); 11-16wk post-term: \( \chi^2 \) test for trend = 16.3, \( p < 0.001 \); 17-24 wk post-term: \( \chi^2 \) test for trend = 7.0, \( p < 0.01 \)).

<table>
<thead>
<tr>
<th>Post-term age</th>
<th>Quality of concurrent motor repertoire</th>
<th>Normal/ Simple MND</th>
<th>Complex MND</th>
<th>Cerebral Palsy</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-10 weeks</td>
<td>Normal</td>
<td>13</td>
<td>4</td>
<td></td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>Abnormal</td>
<td>21</td>
<td>11</td>
<td>11</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>34</td>
<td>15</td>
<td>11</td>
<td>60</td>
</tr>
<tr>
<td>11-16 weeks</td>
<td>Normal</td>
<td>20</td>
<td>1</td>
<td></td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Abnormal</td>
<td>23</td>
<td>16</td>
<td>13</td>
<td>52</td>
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<td></td>
<td>Total</td>
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<td>17-24 weeks</td>
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<td></td>
<td>Total</td>
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<td>10</td>
<td>9</td>
<td>53</td>
</tr>
</tbody>
</table>

Figure 1. Relationship between the quality of the concurrent motor repertoire and neurological findings at school age. For the groups of infants classified as either normal, complex MND or CP at school age, the bars represent the percentage of infants with an abnormal quality of the concurrent motor repertoire (a), in particular a monotonous character (b), a jerky character (c) or a stiff character (d). Differences between groups were tested by the Fisher's exact test. (* = \( p < 0.05 \); ** = \( p < 0.01 \); *** = \( p < 0.001 \)).
Chapter 3

**Prognostic value of combining several qualitative characteristics of the motor repertoire for later complex MND**

At 11-16 weeks post-term, two aspects of the motor repertoire had particularly high prognostic value for the development of complex MND. These were the quality of FMs and the quality of the concurrent motor repertoire. Their prognostic value for neurological findings at school age is shown in Table 4. When FMs were absent, the concurrent motor repertoire was always abnormal, a combination which was highly predictive for the development of CP. When FMs were abnormal, the concurrent motor repertoire was also always abnormal. This combination preceded the development of complex MND in 7 of 11 infants (64%). When FMs were normal, the presence of an abnormal concurrent motor repertoire preceded the development of complex MND (or worse) in 9 of 28 infants (32%). Finally, when both FMs and the concurrent motor repertoire were normal, only 1 infant of 21 (5%) developed complex MND.

Since the different qualitative aspects of the motor repertoire are likely to be interdependent, we performed a multiple logistic regression analysis to investigate which aspects contributed independently to the development of complex MND. Infants who had developed CP were excluded from the analysis, leaving 60 infants, recorded at 11-16 weeks, for further analysis. Aspects of the motor repertoire and clinical data which had shown significant associations with later neurological outcome were entered as predictors: quality of FMs, quality of the concurrent motor repertoire, Apgar score at 5 minutes, presence of prolonged flaring (periventricular leukomalacia grade 1). Only the quality of FMs (LR 4.7; 95% CI 0.99 – 22.5, \( p = 0.05 \)), the quality of the concurrent motor repertoire (LR 14.3; 95% CI 1.1 - 192, \( p = 0.045 \)) and Apgar score at 5 minutes (LR 0.53; 95% CI 0.32 – 0.87, \( p = 0.012 \)) remained in the model. When we combined the qualitative characteristics of the motor repertoire as a single measure, LR for development of complex MND was 2.7 (95% CI 1.5 – 4.9, \( p = 0.001 \)).

**Table 4.** Association between the combination of quality of FMs and the quality of the concurrent motor repertoire, at 11-16 weeks post-term and neurological findings at school age. In case of normal FMs, the quality of the concurrent motor repertoire had additional predictive value for neurological findings at school age. (Chi² test for trend = 5.2, \( p = 0.022 \)).

<table>
<thead>
<tr>
<th>Quality of FMs at 11-16 weeks post-term</th>
<th>Quality of concurrent motor repertoire at 11-16 weeks post-term</th>
<th>Neurological findings at school age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal FMs</td>
<td>Smooth and variable</td>
<td>Normal/ Simple MND 20       Complex MND 1</td>
</tr>
<tr>
<td>Abnormal FMs</td>
<td>Abnormal: monotonous, jerky and/ or stiff</td>
<td>19 8 1 28</td>
</tr>
<tr>
<td>Absence of FMs</td>
<td>Smooth and variable</td>
<td>4 7 11</td>
</tr>
<tr>
<td>Abnormal FMs</td>
<td>Abnormal: monotonous, jerky and/ or stiff</td>
<td>1 12 13</td>
</tr>
<tr>
<td>Absence of FMs</td>
<td>Smooth and variable</td>
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</tbody>
</table>
The quality of the early motor repertoire in preterm infants

Discussion

The present study demonstrates that, in children born preterm, the quality of the motor repertoire at 11-16 weeks post-term is related to clinically relevant, minor neurological dysfunction (complex MND) at 7 to 11 years of age. Both characteristics predictive for an abnormal outcome and characteristics predictive for a normal outcome were identified. Indicative for an abnormal outcome was the presence of abnormal FMs, which was followed by complex MND in nearly two thirds of the cases. Features that were predictive of normal findings at school age were normal FMs in conjunction with a normal concurrent motor repertoire at 11-16 weeks. The quality of FMs also differentiated infants developing complex MND from infants developing CP. FMs were absent at 11-16 weeks post-term in most infants developing CP in contrast to infants developing complex MND.

The assessment of the quality of the motor repertoire at this very young age adds considerably to the individual risk assessment of preterm infants for the development of clinically relevant, complex MND at school age. Clinical characteristics from the perinatal period hardly differentiated infants developing complex MND from infants later classified as normal. Only prolonged flaring (PVL grade 1) and a low Apgar score at 5 minutes were associated with development of complex MND. Prolonged flaring has previously been associated with minor neurological signs and perceptual-motor difficulties in preterm infants, but this was not confirmed in a recent study. Low Apgar scores have also been associated with neurological and developmental disabilities, but prediction in the individual infant is very poor, as is interobserver reliability. In the present study, multiple logistic regression showed the combined measure of qualitative aspects of the motor repertoire at 11-16 weeks post-term to be a strong predictor of later MND.

Our findings are in line with previous studies that have investigated the quality of the motor repertoire at an early age as a predictor for MND. In addition, the present study emphasises the importance of the assessment of FMs. We confirmed the absence of FMs to be highly predictive for the development of CP. In addition, we demonstrated that the presence of abnormal FMs was closely related to the development of complex MND at school age. Previously, abnormal FMs have been associated with poorer fine motor abilities during midpuberty. The biological function of FMs, as a transient, age-specific, distinct form of GMs, is still unclear. It has been speculated that one of the ontogenetic, adaptive functions of these small movements is the optimal calibration of the proprioceptive system. Our findings that abnormal FMs frequently precede clinically relevant abnormalities of coordination, balance and fine motor abilities at school age support this speculation.

Approximately half of the infants who developed complex MND had normal FMs. There must be another explanation for why these infants developed complex MND. In almost all cases, the quality of the concurrent repertoire was abnormal at 11-16 weeks. In particular, a monotonous, but not a jerky or stiff concurrent motor repertoire, was associated with the later development of complex MND. This association was not as strong as the presence of abnormal FMs. Several infants with normal FMs in conjunction with an abnormal concurrent repertoire were later classified as normal. However,
this combination posed a risk of approximately 30% for the development of complex MND. Other investigators have also found that, while reduced variability of spontaneous motility at this young age increases the risk for later neurological abnormalities, a small majority of these infants will develop normally.\textsuperscript{16,17,40} Apparently, reduced variability of the concurrent motor repertoire at this age hampers normal motor development in some but not all infants. Why this is so is an important question. Perhaps a more detailed analysis of specific movement and postural patterns could improve the assessment of the risk for developing complex MND in infants who combine normal FMs with an abnormal concurrent repertoire.

The strongest associations between the quality of early movements and the development of complex MND were seen at 11-16 weeks post-term age. The quality of FMs and of the concurrent repertoire at 6-10 and 17-24 weeks post-term age was less predictive for the development of MND. Previous studies in normally developing children have shown that FMs can be absent before 9 weeks and after 16 weeks post-term age.\textsuperscript{11} This is consistent with the notion that this period can be considered a period of major transformation of the nervous system.\textsuperscript{41} During this transformation many neural functions (postural control, control of visual attention, sucking pattern, social smiling and pleasure vocalisations, motor behavior) change during a relatively short period of several weeks.\textsuperscript{11,41} The present study suggests that the period of 11 to 16 weeks post-term is important not only for the prediction of major neurological sequelae, but also, at least in preterm infants, for the prediction of minor neurological deficits, such as complex MND.

In the present study we were also able to identify infants at low risk for developing complex MND. Normal quality of the concurrent motor repertoire at 11-16 weeks post-term, in combination with normal FMs, was an excellent marker for a normal neurological outcome at school age. This is an important observation for distinguishing between infants who need close surveillance and those who do not. It may also help decide whether early intervention is indicated (e.g. physical therapy), especially when resources are limited.

There are at least two interpretations of our results. The first is that normal FMs in conjunction with a smooth, variable concurrent motor repertoire provide a broad measure of the quality of early central nervous system development. Cortical areas increase their level of activity markedly during the second and third months post-term, as do the cerebellar cortex and the basal ganglia, areas which are involved in networks with important motor, cognitive and behavioral functions.\textsuperscript{42} The presence of normal FMs in conjunction with a normal concurrent motor repertoire may be an index of the quality of early central nervous system development in different areas of the brain. On the other hand, a monotonous motor repertoire might reflect an abnormal development of the cortical and integrative processes that occur at this age.

A second interpretation is that normal FMs in conjunction with a smooth, variable concurrent motor repertoire reflect the role this kind of motor activity plays in the early development of coordination, balance and fine motor abilities. The infants’ exploration of the environment, varying several motor strategies, integrating and refining neural input and output leads to a better neurological
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The absence of a smooth, variable motor repertoire at this age might hamper the infants’ abilities to interact with the world around them during a phase in which sensorimotor activity drives motor development.

There are some limitations to the present study. First, we did not include a term control group. As we do not know how often e.g. an abnormal concurrent motor repertoire occurs in low and high risk term infants, these results cannot be generalised and have to be confirmed in other groups of infants. For this reason, we did not provide data on the sensitivity and specificity of the qualitative assessment of the motor repertoire as described here. A second limitation might be the selection of the infants who had taken part in several earlier studies examining the quality of general movements in several groups at risk for neurological abnormalities. However we consider the children in the present study to be a representative sample of a third level NICU, because both low risk and high risk preterm infants are included.

Conclusions

In conclusion, we found that several aspects of the quality of the motor repertoire at 11-16 weeks post-term were related to complex MND at 7 to 11 years of age in children born preterm. Assessment of the quality of the motor repertoire at this age adds considerably to the assessment of the individual infant’s risk for developing clinically relevant complex MND at school age. The results of the present study suggest the following practical approach for identifying whether or not a preterm infant is at risk for later complex MND. First, at 11-16 weeks post-term, the assessment of the quality of FM is important. Abnormal FMs identify those infants who run a high risk for developing complex MND (60-70%). Normal FMs require a closer look at the concurrent motor repertoire. If FMs are normal at 11-16 weeks post-term, a smooth, variable concurrent motor repertoire is a marker for a normal outcome and the risk for developing complex MND is low (5%). If the quality of the concurrent motor repertoire is monotonous, the risk for developing complex MND is approximately 30%.

Our findings enable the early identification of individual preterm infants at increased risk for development of MND and thus offer opportunities for early intervention and treatment. Moreover, they enable the early identification of individual preterm infants at very low risk for development of MND.
References


