General Movements and Outcome in Children with Birthweights ≤ 500 Grams at Age 5 to 6 Years

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ABSTRACT

Background The prognosis of long-term outcome in the delicate subgroup of preterm infants born with a birthweight ≤ 500 g is difficult. We wanted to determine whether general movements (GMs) correlate with outcome at 5 to 6 years of age in preterm children with birthweights ≤ 500 g.

Methods GMs were assessed up to 20 weeks postterm age in a cohort of infants born consecutively in our unit between 1998 until 2003. A structured neurological examination, the Gross Motor Function Classification Scale, and the Kaufman Assessment Battery Test for Children were applied in surviving children at 5 to 6 years. In relation to long-term outcome, only the postterm GM assessment was analysed.

Results Of 44 infants in total, 19 received immediate life support in the delivery room and were admitted to the NICU (GA 25 weeks [22.3–29.5]; BW 440 g [334–490]). All 9 surviving infants received GM assessment, but only 8 out of 9 infants had postterm assessment; all 9 had outcome assessment at 5 to 6 years. Children with female sex and birthweights > 400 g had better outcomes than those with male sex and birthweights < 400 g. Normal fidgety movements and normal repertoire were associated with normal development at early school age in 3 children, in one child with moderate cognitive impairment and light motor impairment. Pathological fidgety movements or repertoire were associated with abnormal motor development and moderate and severe cognitive impairment in 3 children and with normal development in one child.

Conclusion This study shows that normal fidgety movements at postterm age combined with birthweight and sex may predict normal motor and cognitive outcome in extremely preterm children with birthweights ≤ 500 g.

LIST OF ABBREVIATIONS

ELBW	Extremely low birthweight
ELGA	Extremely low gestational age
IUGR	Intrauterine growth retardation
GMs	General movements
FMs	Fidgety movements
GMFCS	Gross Motor Function Classification System
K-ABC	Kaufman Assessment Battery for Children
MPC	Mental Processing Composite
CBCL	Child's Behaviour Checklist
IVH	Intraventricular haemorrhage

Background

In 2005 and 2010 we published the outcome of children with birthweight ≤ 500 g at discharge and at age 5 to 6 years [1, 2]. Extremely low birthweight (ELBW), extremely low gestational age (ELGA), and intrauterine growth retardation (IUGR) are all risk factors for neurodevelopmental impairment [3–5]. We further wanted to investigate whether general movements (GMs) were predictive of outcome at school age of this subgroup of infants at the edge of viability.

GMs are part of the spontaneous motor repertoire of the foetus and infant up to 5 months [6]. From birth until 2 months of age they have a writhing character; from the beginning of the third month

on they occur as fidgety movements (FMs) [5, 6]. In contrast to neuro-imaging and neurophysiologic evaluations, the assessment of GMs is simple, quick, non-invasive, and cost-effective [6–8]. Recent reviews found a high relationship between the quality of GMs at 8–20 weeks postterm and the infants' neurodevelopmental outcome [7–10]. Prechtl and others showed that abnormalities in the quality of fidgety movements were more predictive of adverse outcomes than abnormal writhing movements [6, 8]. Several authors showed that GMs or GMs in combination with white matter abnormality in MRI scans were a good predictor of cerebral palsy [11–13]. Bruggink et al. showed that the quality of GMs at 3 months corrected age are of prognostic value for intelligence [14]. Some authors found that poor quality of GMs in preterm infants was related to the presence of severe cerebral lesions in the neonatal brain [5, 15–17].

There are some data concerning the predictability of the quality of GMs and neurodevelopmental outcome in extremely low birthweight children [4, 18, 19], but there are none in children with birthweights ≤ 500 g. In order to better inform parents about development of their infants, we wanted to evaluate whether GM assessment results could contribute to the prognosis in early school age of this delicate subgroup of ELBW infants at the edge of viability.

Methods

Subjects

All consecutive inborn infants with a birthweight ≤ 500 g and gestational age ≥ 22.0 weeks born between January 1, 1998, and December 31, 2003, were included in the study. A single outborn infant with a birthweight ≤ 500 g was transferred to our centre within the first 6 h of life and was included in the cohort.

Our original cohort consisted of 44 infants; 13 were stillbirths and 31 were live births. Nineteen of the live births received immediate life support in the delivery room (GA 25 weeks [22.3–29.5]; birthweight 440 g [334–490]); 12 without life support died in the delivery room. Nine infants died during their stay in hospital and one in the first months after discharge home. Nine children survived until follow-up (9 of 19 admitted to the NICU, 47 %; 9 of 44 in total, 20 % [95 % CI 15–27]). Of the surviving children, none had chromosomal aberration or malformation. The outcome results of 7 of the 9 surviving children were included in our former publication [2].

Observation of general movements and routine examinations

Parents were asked whether they wanted to participate in serial video recordings of their infants. Serial video recordings were performed in all infants when they were in a stable state starting at the earliest after the first 2 weeks of life. Recordings were further performed around term and until 10–18 weeks postterm when available. Recordings were performed according to the standard method for GM observation, at least 30 min after feeding and including periods of active wakefulness [20].

To collect a sufficient number of GMs, observation recordings were taken of the infant for about 1 h at preterm and term age. The infant was partially dressed (diaper and body vest), lying in a supine position in his/her incubator, and was filmed from above. The number of recordings of each infant varied from 3 to 8 (median 4). At postterm age, 5–10 min recording time were taken with the infant in the appropriate behavioural state and dressed lightly. The quality of GMs was later assessed by one researcher acting as scorer as described in Einspieler [20] and sent to and assessed a second time by another scorer who is an expert in this field (A. Bos). Both were unaware of the detailed history of the infants. The 3 most complex GMs were taken when the infant was not crying, fussing, being handled, or having a dummy. GMs were described as "normal", "poor repertoire", and "cramped-synchronised". In the postterm phase, the fidgety pattern was described as "normal", "abnormal", "sporadic", or "absent". Multiple GM assessments during preterm and term age are described; for the analysis the worst result was used. In relation to long-term outcome, only the postterm GM assessment was analysed. Postterm assessment could be performed in only 8 out of 9 infants. The interscorer agreement between the 2 scorers was excellent: P. Schulz evaluated sporadic FMs as missing; in all other FM patterns there was full agreement. The decisions from A. Bos were used in the final evaluation.

Serial EEG recordings were scheduled at the earliest after the first 2 weeks of life and subsequently at various times until discharge to monitor ictal activity. Routine brain ultrasound scans were performed according to the standards of the unit until discharge. Assessment was done by the clinical team.

Developmental assessment at age 5 to 6 years

All surviving children were followed and tested. When their child was 4 years of age, parents were contacted to arrange for a follow-up test at the age of 5 to 6 years. At this time, parents were asked to give their informed consent to publish the anonymized data of the GM assessment and the outcome data of their infants. Tests were performed at the age of 5 years in 2 children, and at 6 years in 7 children. One child could not be tested because of multiple impairments. The work described was carried out in accordance with the Code of Ethics of the World Medical Association; ethical approval for examining and reporting the outcome of this cohort of preterm infants had been obtained from the ethics committee of the medical faculty, No. 001/03.

Parents were asked to complete a questionnaire requesting details of the history of their infant, the child's general health, learning development, family and social life, as well as cultural aspects.

A paediatric and neurological examination was done by a paediatric neurologist, who was unblinded to the child's history but blinded to the GM results. The results of this examination were rated as normal, mildly abnormal (minor neurologic signs–such as dysmetria, broad gait, or mild to moderate retardation in motor development), or severely abnormal (severe retardation or cerebral palsy). Furthermore, the weight, length, and head circumference of each child were recorded. The Gross Motor Function Classification System (GMFCS) [21] was performed to assess mobility.

The Gross Motor Function Classification System (GMFCS) is normally used to describe gross motor function in cerebral palsy with a range of categories: "most able" (Level 1) to "most limited" (Level 5). Normal mobility is represented by a score of 1, mild immobility by 2 (locomotion possible but abnormal), moderate immobility by 3, severe immobility by 4, and the lack of mobility by 5.

The assessment of visual perception and hearing ability in the children was based on the records of ophthalmologists and paediatric audiologists. Severe visual impairment was defined as a refractory error of more than ± 10 diopter. A visual acuity after best-possible correction for ametropia by refractive lenses of < 20/200 (one tenth of normal vision) was defined as blindness. Severe hearing disability was defined when a hearing aid for one or both ears was necessary.

Cognitive function was evaluated by a child psychologist with the Kaufmann Assessment Battery for Children (K-ABC) [22]. The K-ABC comprises the mental processing composite (MPC), a global measure of cognitive ability that can be interpreted similarly to an IQ test, and the achievement scale, assessing knowledge of facts, language, and skills related to needs in school. The MPC consists of two subscales, sequential processing and simultaneous processing. The K-ABC was standardized in 1992 to a mean of 100 and an SD of 15 in a German reference population.

Parents were also asked to report their child's behaviour by filling in the Child Behaviour Checklist (CBCL) [23]. The CBCL checklist was developed in 1966 and asks parents to answer questions grouped in eight categories to describe child behaviour: social withdrawal, somatic complaints, anxiety/depression, social problems, attention problems, delinquent behaviour, and aggressive behaviour. The test for 4- to 18-year olds was used. Responses are recorded on a Likert scale: 0 = not true, 1 = somewhat or sometimes true, 2 = very true or often true. The school-age checklist contains 120 questions. Evaluation was performed by one researcher summing scores for each category and forming summary scores for internalising and externalising problems.

Composite outcome

Development was recorded as normal when the results of neurologic examination, mobility and cognitive development (MPC > 85) were all normal in the absence of severe visual and hearing impairment. Mild developmental disability was defined as any abnormal result of neurologic examination with normal mobility and/or an MPC of 71–85 and the absence of severe visual and hearing impairment. Moderate disability included any abnormal neurologic examination result with/without mild immobility and/or an MPC of 50–70 and/or severe visual impairment. Severe disability was defined as any abnormal neurologic examination result with moderate or severe immobility or the lack of mobility and/or severe cognitive impairment with an MPC < 50 and/or severe hearing impairment (hearing aid) and/or blindness.

Analysis

Quantitative data are given as median and range, qualitative data by counts and percentages. Confidence intervals (95 % CI) were calculated. Analyses were performed with Sigma Plot®, Version 12.0 (Systat Software Inc., San Jose, California, USA). Logistic regression taking into account several confounding factors like intraventricular haemorrhage (IVH) and bronchopulmonary dysplasia (BPD) was not performed, because the group of infants was too small to receive valid results.

Results

Baseline characteristics of surviving children of the cohort are given in ▶ **Table 1**.

All but one infant was treated with antenatal steroids, all but one had BPD, and 4 were treated by laser coagulation because of retinopathy of prematurity (ROP) III + . Five of them were treated with indomethacin because of patent ductus arteriosus (PDA), and 2 of those ultimately had ligation of their PDA. None of the infants had ictal activity. Head ultrasounds showed no IVH III or higher, and half of the infants had no IVH at all.

GM assessment showed "poor repertoire" in all assessments at preterm age. This pattern also dominated assessment at term age. The postterm assessment of the infants at 3 to 4 months could be performed in only 8 out of 9 infants and showed normal FMs in four infants and abnormal ones in a further four infants (▶ **Table 2**).

No infant with normal FMs had IVH. Three infants with IVH II showed moderate developmental disability in 2 cases and normal development in one case. One infant with IVH I had severe developmental disability, and 5 infants with no IVH developed normally in 3 cases and showed moderate developmental disability in 2 cases.

▶ **Table 3** shows the main outcome data. Two of the small-for-gestational-age (SGA) children had had catch-up growth, but body weight and head circumference of 7 children were below the 10th percentile. Five children had a normal neurologic examination and 3 children presented with a mildly abnormal result. One child had a severely abnormal result reflecting multiple impairments: severe retardation in motor development, moderate immobility, blindness, and hearing impairment requiring a hearing aid. None of the followed children had cerebral palsy. Half of the children showed a

▶ **Table 1** Baseline characteristics and neonatal morbidity of tested infants (n = 9).

Gestational age	
Median (minimum-maximum), wk	25.0 (22.9–27.9)
Birthweight	
Median (minimum-maximum), g	418 (350–490)
Female gender, n (%)	6 (67)
Multiple, n (%)	0 (0)
Clinical risk index for babies (CRIB) score	
Median (minimum-maximum)	10,3 (8–13)
Antenatal steroids, n (%)	8 (89)
Bronchopulmonary dysplasia, n (%)	8 (89)
Intraventricular haemorrhage, n (%)	
≥ III, n (%)	0 (0)
II both sides	1 (11)
II one side	2 (22)
I	1 (11)
none	5 (56)
Periventricular leucomalacia, n (%)	0 (0)
Retinopathy of prematurity ≥ III, n (%)	4 (44)
Necrotising enterocolitis Bell stage ≥ 2, n (%)	0 (0)

mental processing composite (MPC) in the normal range, but 4 had an MPC between 50 and 70. All but one infant with a birthweight > 400 g had a normal outcome (one infant with moderate developmental disability), whereas all infants with birthweights below 400 g had an abnormal outcome. All infants with a normal outcome were female (▶ **Table 2**).

With respect to long-term outcome, only the postterm GM assessment was analysed. Normal fidgety movements and normal repertoire were associated with normal development at age 5–6 years in 3 children, and in one child with moderate cognitive impairment (MPC < 70) and mildly abnormal motor development (▶ **Table 2**). Pathological fidgety movements or repertoire were associated with abnormal motor development and moderate and severe cognitive impairment in three children (2 × MPC < 70, 1 × < 50) and with normal development in one child (▶ **Table 2**). The blind child showed increased jerkiness, an attitude previously described by Prechtl [24].

CBCL assessment revealed anxiety and social withdrawal in one girl and antisocial and aggressive behaviour in one boy; all other children performed normally. All but 2 mothers had a middle school education, while the 2 others had no training qualification. Only one family had further children after the infant included in this study, 2 children had older siblings. Seven of the 9 families had a positive view of the future, 6 of 9 said that the birth of their infant had changed their lives completely.

Information concerning outcome at the age of 15 to 20 years was obtained from 5 of the 9 children; one had moved abroad and 3 did not answer. Two of the 5 teenagers who provided information with normal outcome had school results in the normal range and started working at age 16. They have no impairments. All three children with moderate and severe impairments attended a special-needs school and work in special institutions. They still live at home, and the severely impaired child lives in an institution for disabled persons.

Discussion

This is the first study to investigate the correlation of GM assessment with outcome at 5–6 years in children with birthweights ≤ 500 g. With respect to long-term outcome, only the postterm GM assessment was analysed. Despite intrauterine growth retardation and low gestational age, 4 of the 9 surviving children had normal development. Combined motor and cognitive impairment was more often associated with abnormal GMs at postterm age, whereas normal GMs and normal repertoire at postterm age were associated with a normal outcome in the majority of children in this small group. Birthweight and sex seem to be a predictor of outcome in our cohort, whereas IVH does not seem to be a predictor.

Upadhyay et al. recently published a retrospective review of all infants admitted to their NICU with a birthweight ≤ 500 g in the last 20 years [25]. They found a survival rate of about one third and age-appropriate neurological development at 24-month follow-up in 33 % of survivors in their cohort at the edge of viability. Our group included 9 surviving children all of them being ELGA and SGA infants ≤ 500 g birthweight. The survival rate of surviving infants in our small cohort was higher compared to the results of Upadyay, the rate of normal outcome of surving infants at age 5 to 6 years was higher than Upadhyay reported at 24-month follow-up. Inoue recently published early-outcome data on infants with birthweights < 500 g [26], showing survival of 55 % but a high rate of major morbidities. In contrast to our study, this study included a large group of 22- and 23-weekers and does not report long-term outcome.

Because a 500 g birthweight falls within the 10th percentile at a gestational age of 24 weeks [27], almost all of our infants are IUGR infants. Both factors, i. e., extreme prematurity and IUGR, may have influenced our study results. Birthweight seems to be a predictor of outcome in our small study, because all infants with birthweights below 400 g in our small group had an abnormal outcome and all but one with a birthweight > 400 g had a normal outcome.

▶ **Table 2** General movements and neurologic outcome at age 6 years (n = 9).

		GM					
Outcome	**n**	**Preterm**	**Term**	**Postterm**	**Sex**	**GA**	**BW**
Normal	4	PR	CS	Normal FMs, normal repertoire	f	27 + 6	430
		N→PR	N	Normal FMs, normal repertoire	f	24 + 6	490
		PR	–	Sporadic FMs, monotonous repertoire	f	22 + 6	480
		PR	PR	Normal FMs, normal repertoire	f	24 + 6	400
Moderate developmental disability	4	-	PR	Sporadic FMs, monotonous repertoire	f	26 + 1	364
		PR	PR	Sporadic FMs, monotonous repertoire	m	24 + 0	350
		PR	–	Normal FMs	m	24 + 6	490
		N→PR	–	–	f	24 + 3	390
Severe developmental disability	1	PR	PR→CS	Normal FMs, increased jerkiness	m	25 + 2	370

GA, gestational age; BW, birthweight; N, normal; CS, cramped synchronized; PR, poor repertoire; PR→N, poor repertoire normalising during study period; N→PR, normal repertoire changing to poor repertoire; PR→CS, poor repertoire changing to cramped synchronized pattern; FMs, fidgety movements; f, female; m, male

Sex also seems to be a predictor of outcome in this group, because all infants with a normal outcome were female (▶ **Table 2**)

Results of low-grade IVH on later outcome are controversial. There are reports of no difference in outcome at 2 and at 18 years when very preterm infants with and without low-grade IVH are compared [28, 29] , but there are also reports which found an impact of low-grade IVH on long-term neurodevelopmental outcome [30]. In our study, 4 infants had low-grade IVH, 2 of whom developed moderate and one severe developmental disability; one developed normally. Of 5 infants with no IVH, 3 developed normally and 2 had a moderate developmental disability at 5 years. Thus IVH does not seem to be a good predictor of outcome in our small study.

Outcome at school age in our group was in accordance with outcome at teenager and young adult age in the 5 former preterm infants who could be contacted.

▶ **Table 3** Growth and neurosensory development at follow-up at 5 to 6 years (n = 9).

Growth (n = 9)	**n (%)**
Weight	
> 10th percentile	2
< 3rd percentile	5 (56, 95 % CI 17–95)
Length	
> 10th percentile	1 (11)
< 3rd percentile	2 (22)
Head circumference	
> 10th percentile	2 (22)
< 3rd percentile	5 (56)
Neurologic examination (n = 9)	n (%)
Normal	5 (56)
Abnormal	4 (44, 95 % CI 5–83 %)
Mildly abnormal	3 (58)
Severely abnormal	1 (16)
GFMCS	
Abnormal (score 3)	1 (11)
Visual impairment (n = 9)	n (%)
Severe myopia	2 (22)
Blindness	1 (11)
Hearing impairment (n = 9)	
Requiring hearing aid	2 (11)
Cognitive development (n = 8)	n (%) [range]
Mental Processing Composite (MPC)	75 [50–102] (median) [range])
MPC > 85	4 (50) [86–102]
MPC < 85	4 (50) [50–63]
Composite outcome (n = 9)	n (%)
Normal development	4 (44, 95 % CI 5–83 %)
Mild developmental disability	0
Moderate developmental disability	4 (44)
Severe developmental disability	1 (11)

In our group of infants, only one infant showed normal GM patterns at preterm and term age; this child had a normal outcome. Poor repertoire was the dominating pattern at both time points, a finding that had been reported by Albers and Nakajma, who showed that this GM pattern did not automatically lead to abnormal neurological development [31, 32]. De Vries later found that GM patterns in the first 14 days fluctuated substantially and that poor repertoire GMs were observed most frequently [33, 34]. In another study, she found that abnormal GMs are common in ELBW infants at term age and do not imply later impaired neurological outcome [18]. De Vries hypothesized that many physiological and chemical changes which influence brain function take place in ELBW infants during early life. Because of the fact that GMs at preterm and term age do not predict later outcome, only the postterm GM assessment was analysed in relation to long-term outcome.

In their review which included 17 studies, Burger and Louw found that sensitivity and specificity values of GMs increased from the preterm and term period and reached the highest values at 8–20 weeks postterm [7]. Einspieler stated that at postterm age, normal intermittent or continual FMs correlated well with outcome [35], whereas the role of sporadic FMs present at 3 to 4 months did not indicate a milder type of cerebral palsy (CP) in a group of infants developing CP [35]. In a review she concluded that abnormal, absent, or sporadic FMs indicate an increased risk for later neurological dysfunction [36]. She further pointed out that many researchers grouped sporadic FMs as absent FMs, just as scorer 1 had done in this study. This explains the only disagreement between the two scorers well. The presence of sporadic FMs was associated twice with abnormal outcome and one time with normal outcome in our group. Besides the FM pattern, concurrent movements should be evaluated. Fjørtoft showed that monotonous, jerky, and/or stiff gross movements at 3–4 months postterm predicted a poor motor outcome at 10 years [37]. Increased jerkiness could result from an altered course of normal development of FMs described by Prechtl [24]. Monotonous repertoire or increased jerkiness was mostly associated with abnormal outcome in our study. However, one child born at 22 weeks gestation with sporadic FMs and monotonous repertoire developed normally.

More common than motor impairment in ELBW infants is cognitive impairment. Recent studies on preterm infants demonstrate that abnormal GMs also reflect impairments of brain areas involved in cognitive development [37]. Spittle et al. showed that abnormal GMs at 3 months were associated with worse motor, cognitive, and language outcomes at 2 and 4 years [19]. Bruggink et al. showed that the quality of GMs during the early postterm period was a marker for intelligence at school age [13]. Grunewaldt et al. demonstrated that ELBW infants with abnormal GMs at the age of 3 months had a lower working memory index and more behavioural problems as well as reduced brain volumes on MRI scans at age 10 years [4]. In our group all assessed children with motor impairment also had cognitive impairment. The mental processing composite (MPC) of these children was between 50 and 63. All of them had shown either sporadic FMs and monotonous repertoire or normal FMs over a very short time or normal FMs with increased jerkiness at the postterm age of 3 months. The one who showed normal FMs over a very short time developed behavioural problems in addition to light motor and severe cognitive impairment. Thus the results

published by Einspieler, Bruggingk, and Grunewaldt may also apply to children born with birthweights ≤ 500 g.

Although the results of studies reporting on intrauterine growth retardation (IUGR) infants are conflicting, the main results show an increased risk for mild neurodevelopmental abnormalities with cognitive disorders and behavioural problems more so than motor disturbances [5]. Microcephaly and a lack of head catch-up growth are risk factors for abnormal development [5]. Veelken found a higher frequency in minor neurological disabilities in preterm IUGR infants < 1500 g birthweight [38], McCarton an increased risk for neurodevelopmental impairment in preterm IUGR infants < 2500 g birthweight [39], and Kok more gross-motor dysfunction and more minor neurological dysfunction in IUGR infants < 32 weeks gestation [40]. Zuk demonstrated that the incidence of normal GMs was lower in the growth-retarded group < 2500 g birthweight than in AGA controls and correlated well with outcome at 2 years [41]. Bos demonstrated that in particular the quality of FMs was a marker for neurological outcome at 24 months in preterm infants with a birthweight below the 5th percentile [42]. Four of the IUGR infants of our cohort had developed normally despite a lack of catch-up of head growth in 2 of them.

The main limitation of this study is the small number of surviving infants until the age of 6 years whose outcome could be assessed and correlated with GM assessment. Unfortunately in one child no FM assessment had taken place. A further disadvantage is that GM assessment was possible in only one of the 3 centres which contributed patients to the original cohort of infants with birthweights ≤ 500 g. In addition, this cohort consisted of mainly IUGR infants, and all infants with serious intracerebral morbidity such as severe IVH had died during their first stay in hospital.

The strengths of our study are that the infants were both ELBW and IUGR infants at the same time, that the study group was therefore homogeneous, that all surviving infants were included in the follow-up assessment, and that the follow-up took place at the start of school age when subtle neurologic dysfunction can also be detected.

Conclusion

Our results on GM assessment and outcome in this small cohort of infants born at the edge of viability are similar to those of other published studies in ELBW and IUGR infants with higher birthweights. GM assessment at 8–20 weeks postterm may therefore also predict outcome in infants with birthweights ≤ 500 g and may help in counselling parents. The combination of GM assessment, birthweight, and sex may even predict outcome better than GM assessment alone.

Conflict of Interest

The authors declare that they have no conflict of interest.

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