Quality of general movements in infancy is related to neurological dysfunction, ADHD, and aggressive behaviour

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The quality of general movements (GMs) was assessed repeatedly during the first postnatal months in a mixed group of 52 children at either low or high risk for neurodevelopmental disorders. In addition, all children were reexamined at 4 to 9 years. The follow-up assessment consisted of a neurological examination and an evaluation of behaviour by means of parental questionnaires. The quality of GMs changed frequently, to stabilize in the final phase. The final GM phase is that of the so-called fidgety GMs which occurs between 2 and 4 months postterm. The quality of the fidgety GMs predicted outcome very well. Definitely abnormal GMs were associated with a high risk for the development of cerebral palsy, whereas mildly abnormal GMs were associated with the development of minor neurological dysfunction, attention-deficit–hyperactivity disorder, and aggressive behaviour.

During the past few years it has become clear that the quality of general movements (GMs) of young infants is a powerful predictor of the development of neurological disorders such as cerebral palsy (CP) (Ferrari et al. 1990, Prechtl et al. 1993, Hadders-Algra 1996). GMs are complex movements, which involve head, trunk, arms, and legs. They arise during early fetal life (De Vries et al. 1982) and persist until 3 to 4 months after term age (Hopkins and Prechtl 1984, Hadders-Algra and Prechtl 1992). Normal GMs are characterized by fluency, variation, and complexity (Prechtl 1990). Their form changes with increasing age. Before 36 to 38 weeks' postmenstrual age (PMA), GMs show a great variation in movement trajectory, speed, and amplitude. These GMs are called preterm GMs. Around 36 to 38 weeks' PMA, preterm GMs are replaced by writhing GMs which are slower and more powerful than preterm GMs and show less involvement of the trunk (Hadders-Algra and Prechtl 1993, Hadders-Algra et al. 1997). At the end of the second month postterm (46 to 48 weeks' PMA) another transition in GM form takes place (Hopkins and Prechtl 1984, Hadders-Algra and Prechtl 1992). The writhing character disappears and the movements become fidgety; a continuous stream of tiny, elegant movements occurring irregularly all over the body.

Two forms of abnormal GMs have been distinguished on the basis of the analysis of video and EMG recordings: (1) mildly abnormal GMs which lack fluency, but still show some movement complexity and variation; and (2) definitely abnormal GMs which lack fluency, complexity, and variation altogether (Hadders-Algra et al. 1997). The persistent presence of definitely abnormal GMs during the three (in preterm infants) or two (in term infants) GM phases puts an infant at high risk (70 to 80%) for the development of a neurological disability (Ferrari et al. 1990, Prechtl et al. 1993, Bos 1997). Also the presence of definitely abnormal GMs at fidgety-GM age, implying the total absence of the normal fidgety dance, indicates a high risk for the development of CP (Hadders-Algra et al. 1997, Prechtl et al. 1997). Little is known about the significance of mildly abnormal GMs for the child's future development. Our previous EMG study on a small group of high-risk infants ($N=16$), who were followed until 1 year 6 months of age, suggested that the presence of mildly abnormal GMs might be related to the development of minor neurological dysfunction (MND) (Hadders-Algra et al. 1997). Another issue which deserves clarification is the significance of changes in GM quality during postnatal life. Such changes have been reported repeatedly (Ferrari et al. 1990, Prechtl et al. 1993, Bos et al. 1997), but systematic accounts of their occurrence and significance are lacking.

The aim of the present study is threefold. First, to report the occurrence and significance of changes in GM quality during early postnatal life. Second, to clarify the significance of mildly abnormal GMs for the child's neurological and behavioural development beyond the age of 1.5 years. To this end, a mixed group of 52 high- and low-risk children, whose GMs had been recorded repeatedly during early postnatal life, was reexamined at school age (4 to 9 years). The assessment at school age consisted of a standardized and age-specific neurological examination and an evaluation of behaviour by means of parental questionnaires. Special attention was paid to the presence of attention-deficit–hyperactivity disorder (ADHD), because a strong correlation exists between ADHD and minor motor

dysfunctions (Gillberg and Rasmussen 1982, Hadders-Algra et al. 1988b, Losse et al. 1991, Soorani-Lunsing et al. 1994). The third aim was to compare the power of GM assessment and that of the infant neurological examination to predict the development of CP, MND, and ADHD.

Method

Fifty-two children were enrolled in the study. Their parents gave informed consent and the procedures were approved by the Ethics Committee of the University Hospital, Groningen, The Netherlands. All children had participated in our EMG studies on the development of normal and abnormal GMs (see Hadders-Algra et al. 1992, 1997). Twenty-eight children were born at term between 1988 and 1992. They were free from pre- and perinatal complications, and therefore considered to be at low risk for neurodevelopmental disorders. The remaining 24 children were considered to be at high risk for neurodevelopmental disorders. They were born between 1991 and 1993. Six of them were born at term and had had hypoxic–ischaemic encephalopathy (one at Sarnat stage 1, four at stage 2, one at stage 3) (Sarnat and Sarnat 1976). The other 18 high-risk children were born preterm at gestational ages ranging from 26 to 36 weeks (median 30 weeks). Additional clinical information, including data on the neonatal ultrasound scans of the brain, is provided in Table I. Serial brain ultrasound scans were only performed in the high-risk children. The preterm infants were scanned weekly during the first 3 to 4 weeks after birth. In the high-risk term infants three to five ultrasound scans were made during the first 2 weeks. Additional scans were performed at ages guided by previous sonographic findings until the age of 2 to 4 months postterm. Periventricular haemorrhages (PVH) and leukomalacia (PVL) in the preterm infants were classified according to Levene et al. (1982) and De Vries et al. (1992), respectively. The ultrasound findings were then classified as normal (no haemorrhages and/or echodensities lasting <1 week), mildly abnormal (PVL grade 1, PVH grade 1 or 2), and definitely abnormal (PVL grade 2 or 3, PVH grade 3, cortical infarction).

The children were assessed at various times during the first postnatal months, the number of examinations per infant varying from three to eight (median four). The assessment series started 2 to 4 weeks (median 3 weeks) after birth in the low-risk group, and as soon as the condition of the infant permitted transportation to the EMG-recording room, which happened 1 to 6 weeks (median 2 weeks) after birth in the high-risk group. The low-risk group was recorded at 4-week intervals until 3 to 4 months after birth. The high-risk

Table I: Clinical data of studied children

	Low risk	*High risk*	
	N=28	*Term (hypoxic–ischaemic encephalopathy) N=6*	*Preterm N=18*
Neonatal data			
Gestational age at birth, range (median)	38–43 (40)	38–43 (40)	26–36 (30)
Birthweight (g) (mean ± SD)	3467±499	3014±394	1438±548
SGA, birthweight <2.3% (*N*)[a]	0	1	3
Sex (M/F)[b]	17/11	2/4	11/7
Ultrasound findings (*N*)[c]			
Normal		3	4
Abnormal		3	
PVL, grade 1			10
PVL, grade 2			2
PVL, grade 3			1
Posthydrocephalic state			1
Nr of early postnatal assessments, range (median)			
At preterm-GM age			0–3 (1)
At writhing-GM age[b]	0–2 (2)	1–3 (3)	1–3 (2)
At fidgety-GM age[b]	2–4 (3)	1–3 (2)	1–3 (2)
At follow-up			
Age range (median) (y)[d]	4.5–9.0 (7.5)	4.0–5.0 (4.5)	4.0–5.5 (4.5)
Nr of children in social class (*N*)[b, e]			
Low	0	0	3
Lower-middle	13	2	5
Upper-middle	10	4	7
High	5	0	3

[a] SGA, small for gestational age, birthweight <2.3% of Kloosterman (1970) growth curves.
[b] Mann–Whitney: no significant differences between groups.
[c] Ultrasound findings: PVL, periventricular leukomalacia according to de Vries et al. (1992), four infants with PVL also had a periventricular haemorrhage grade I–II; Term hypoxic–ischaemic encephalopathy group: infants classified as normal did exhibit cerebral oedema, those with abnormal findings showed abnormalities in cerebral cortex (*N*=2) or cerebellum (*N*=1).
[d] Mann–Whitney: difference between low- and high-risk groups: P<0.01.
[e] Social class according to maternal occupation (Sixma and Ultee 1983).

children were recorded every 2 to 3 weeks during their stay in the hospital. After discharge home or to another hospital, the high-risk children were recorded every 4 to 6 weeks until the final examination at the age of 3 to 4 months postterm. The number of postnatal assessments in the different groups is shown in Table I.

Each session consisted of a video recording of spontaneous motility in supine position, while multiple surface EMGs were recorded. In the present study, only the video data were used. The recordings lasted 20 to 40 minutes, depending on the behavioural state of the infant. To prevent a confounding effect of behavioural state on GM quality (Hadders-Algra et al. 1993), only movements during an awake, active, non-crying behavioural state were analysed. This strategy could be followed only in infants with fully developed behavioural states, i.e. from 38 weeks' PMA onwards (Nijhuis et al. 1982). Before this age, GMs were excluded from the analysis when they occurred during crying or during periods with many signs of REM-sleep activity, such as eye movements, irregular breathing, or small hand and face movements. The duration of GM activity in an adequate state was at least 2 minutes. The quality of the GMs was assessed by the two authors independently, one of whom (AMCG) was blind to the clinical data of the infants. The movements were classified into normal, mildly abnormal, and definitely abnormal GMs (Table II, see Hadders-Algra et al. 1997). Interscorer agreement of all GMs was very good (κ=0.82; Landis and Koch 1977). In instances of disagreement, the movements were reanalysed and discussed until consensus was reached. Before each video recording, a standardized neurological examination was performed, using the techniques of Touwen (1976) and Prechtl (1977), with age-specific adaptations of the norms for the assessments before term age. The neurological findings were summarized as normal, mildly abnormal, or definitely abnormal (see Jurgens-Van der Zee et al. 1979).

All children enrolled in the infant assessments participated in the follow-up in 1997. The age at follow-up varied between 4 and 9 years. Due to the design of the EMG studies, in which we first evaluated characteristics of normal movements and then those of abnormal movements, the age at follow-up of the low-risk children was significantly higher than that of the high-risk group (Table I). Each follow-up assessment consisted of a neurological examination and an evaluation of the child's behaviour. For the neurological examination, we used standardized and age-specific neurological assessments according to Hempel (1993) for children <5 years, and Touwen (1979) for children ≥ 5 years. These assessment techniques are specially designed for the evaluation of MND, such as mild abnormalities in muscle tone, choreiform dyskinesia, mild problems with coordination, and fine manipulative abilities. On the basis of the neurological examination, the children were grouped into three categories: (1) neurologically normal, (2) MND, the presence of which resulted in an impairment or disability but did not lead to a disabling condition, and (3) CP (Aicardi and Bax 1992) which resulted in a disability (WHO 1980). The neurological examination was recorded on video. The video recordings were used to assess the presence of MND in the children without CP by the two authors independently. Again, AMCG was totally unaware of the child's history. The assessment of muscle tone and reflexes could not be double-checked in this way. For the other aspects of neuromotor behaviour, interscorer agreement was good: coordination problems, κ=0.75; dysfunctions of fine manipulative ability, κ=0.70; choreiform dyskinesia, κ=0.98 (Landis and Koch 1977). In cases of disagreement, the video assessment was reanalysed and discussed until agreement was achieved. In addition, the video recordings were used to score the fluency of motility, in particular the fluency of leg and trunk movements during walking (two items), and of trunk movements during sitting and standing (two items; see Hempel 1993). Each of the four fluency items was rated on a 2-point scale (0=movements not fluent at all, but jerky and/or stiff; 1=moderately fluent movements; 2=nicely fluent movements). A total fluency score was subsequently computed by adding the four fluency scores (maximum 8 points).

Table II: Definitions of GM characteristics

Parameter	*Normal GMs*	*Mildly abnormal GMs*	*Definitely abnormal GMs*
GM complexity The infant actively produces frequent changes in movement direction of participating body parts. Changes in movement direction are brought about by continuously varying combinations of flexion–extension, abduction–adduction and endorotation–exorotation of participating joints	++	+	–
GM variation Spatial diversity in movement patterns of participating body parts within a single GM and/or between consecutive GMs	++	+	–
GM fluency Presence of smooth, supple, and graceful movements. Fluency in particular points to velocity profile of movements. Fluent GMs are characterized by a normal distribution of movement velocity, whereas in non-fluent GMs an excess of slow and/or fast movements is present	++	–	–

– absent; + present to a limited extent; ++ fully present.

Behaviour was evaluated by means of three parental questionnaires (Table III). First, we used the standard questionnaire of the Groningen Perinatal Project (e.g. Hadders-Algra et al. 1988b). Second, the parents filled in the CBCL (Achenbach 1991). This resulted in a Total Score, a score on Externalizing and Internalizing Behaviour, and various Problem Scores. Third, as we were particularly interested in the presence of ADHD and because we thought that the CBCL Attention Problems score did not quite fit ADHD behaviour, we adapted the criteria list for ADHD in the DSM-IV manual (American Psychiatric Association 1994) into a parental questionnaire. The DSM questionnaire resulted in three outcome parameters: (1) 'inattention', when the child had ≥ six positive criteria of the nine denoting inattention; (2) 'hyperactivity', when the child had ≥ six positive criteria of the nine describing hyperactivity/impulsivity; (3) ADHD, when the child had scored either 'inattention' or 'hyperactivity/impulsivity'. In addition, information was collected on intercurrent disorders and social class (Table I).

For most group comparisons, non-parametric tests were used, such as the Fisher exact, χ^2, and the Mann–Whitney U tests. Occasionally the Student t test could be applied (for example, for the movement-fluency score). Multivariate statistics were used to evaluate the contribution of mildly abnormal GMs to behavioural development: a multiple regression analysis for continuous outcome parameters and logistic regression analysis for dichotomous outcome variables. Throughout the analyses, differences with a P value ≤0.05 were considered to be statistically significant (two-tailed testing).

Results

CHANGES IN GM QUALITY

GM quality within a GM phase was relatively stable (Table IV) and did not change before 38 weeks' PMA in any one of the three preterm infants in whom multiple recordings were available. In the writhing-GM phase, 35 children had multiple recordings. GM quality changed in four children: definitely abnormal to mildly abnormal in two children, mildly abnormal to definitely abnormal in one, and normal to mildly abnormal in

Table III: The behavioural questionnaires

Groningen Perinatal Project Questionnaire – GPPQ (Hadders-Algra et al. 1988)			
Information asked in an age-specific, comparative way: 'All children of this particular age are sometimes...., do you regard your child as more.... or less....., or don't you see any difference'.			
Irritable	Hyperactive	Shy, withdrawn	Headstrong
Difficult to concentrate[a]	Anxious	Temper tantrums	Distractible[a]
Easily frightened	Difficult	Clumsy	
Child Behavior Check List – CBCL (Achenbach 1991)			
Problem scores [b]			
Withdrawn	Social Problems	Delinquent Behaviour	Aggressive Behaviour
Somatic Complaints	Thought Problems	Anxious/Depressed	Attention Problems
Sexual Problems			
Externalizing Score			
Internalizing Score			
Total Score			
DSM Questionnaire for Attention-Deficit/Hyperactivity Disorder (based on DSM-IV, American Psychiatric Association 1994)			
Criteria for inattention[c]			
Often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities			
Often has difficulty sustaining attention in tasks or play activities			
Often does not seem to listen when spoken to directly			
Often does not follow through on instructions and fails to finish schoolwork, chores, or play			
Often has difficulty organizing tasks and activities			
Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework)			
Often loses things necessary for tasks or activities (e.g. toys, school assignments, pencils, books or tools)			
Is often easily distracted by extraneous stimuli			
Is often forgetful in daily activities			
Criteria for hyperactivity /impulsivity[c]			
Often fidgets with hands or feet or squirms in seat			
Often leaves seat in classroom or in other situations in which remaining seated is expected			
Often runs about or climbs excessively in situations in which it is inappropriate			
Often has difficulty playing or engaging in leisure activities quietly			
Is often 'on the go' or often acts as if 'driven by a motor'			
Often talks excessively			
Often blurts out answers before questions have been completed			
Often has difficulty awaiting turn			
Often interrupts or intrudes on others (e.g. butts into conversations or games)			

[a] Information supplied in three classes: no; yes, a little; yes, very much.
[b] 0=does not apply at all; 1=applies to a little extent; 2=applies rather well; 3=applies extremely well. A criterion was considered to be present with a score 2 or 3.
[c] 0=does not apply; 1=does apply to some extent; 2=applies very well.

one. Forty-eight children had multiple recordings during the fidgety-GM phase. Only one of them showed a change in GM quality; from abnormal to mildly abnormal.

GM quality changed considerably more frequently during the ages at which GM form changes during normal development (Table IV). Four of the 18 preterm children showed a change in movement quality concurrent with the transition from preterm to writhing GMs. Movement quality in these four children deteriorated (Fig. 1). Also during the transitional period from writhing to fidgety GMs, movement quality changed in a quarter of the infants (13 of 52). At this transition, movement quality in general improved, changing from definitely abnormal into mildly abnormal, or from mildly abnormal into normal (Fig. 1).

Owing to GM quality being relatively stable within a GM phase, we awarded each infant one GM quality per GM phase. This 'filtered' GM quality consisted of the most frequently occurring classification or, in case of an equal frequency of two classifications, the better quality of the two. A similar filtering procedure was followed for the results of the neurological examination.

GM QUALITY AND NEUROLOGICAL CONDITION AT FOLLOW-UP

No low-risk but eight high-risk children developed CP (Table V). MND also occurred more often in the high-risk group (10 of 24 children) than in the low-risk group (three of 28 children). No significant contribution of intercurrent disorders to neurological development could be established.

Most children with MND had a combination of mild abnormalities in muscle-tone regulation and dyscoordination, including balance problems (Table V). The mildly abnormal muscle-tone regulation consisted of a mild hypotonia, a mild hypertonia, or an unstable muscle tone, which fluctuated between mild hypotonia and mild hypertonia. The latter two forms of muscle-tone dysregulation were associated with a significantly reduced fluency of leg and trunk movements (mean total fluency score in children with a normal muscle tone or a mild hypotonia 6.9±1.2, in children

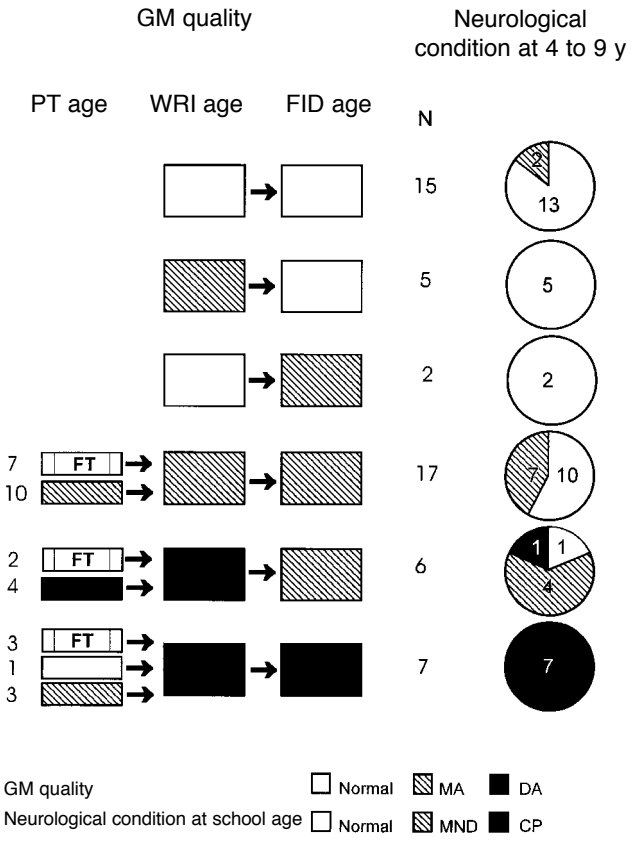

Figure 1: *GM quality during three GM phases and neurological condition at 4 to 9 years. Figure displays developmental trajectories in groups of children. For example, bottom row illustrates development of seven children, who showed definitely abnormal GMs during writhing and fidgety periods and who developed CP. Three of those seven were born at term (FT) and four were preterm. Three of these preterm children had shown mildly abnormal GMs during preterm-GM phase and one had shown normal GMs (sudden and unusual change from normal to definitely abnormal GMs being due to a streptococcal meningitis at week 36). PT age, period of preterm GM, <37 weeks' PMA; WRI age, period of writhing GMs, 38 to 47 weeks' PMA; FID age, period of fidgety GMs, >47 weeks' PMA. GM quality: MA, mildly abnormal; DA, definitely abnormal.*

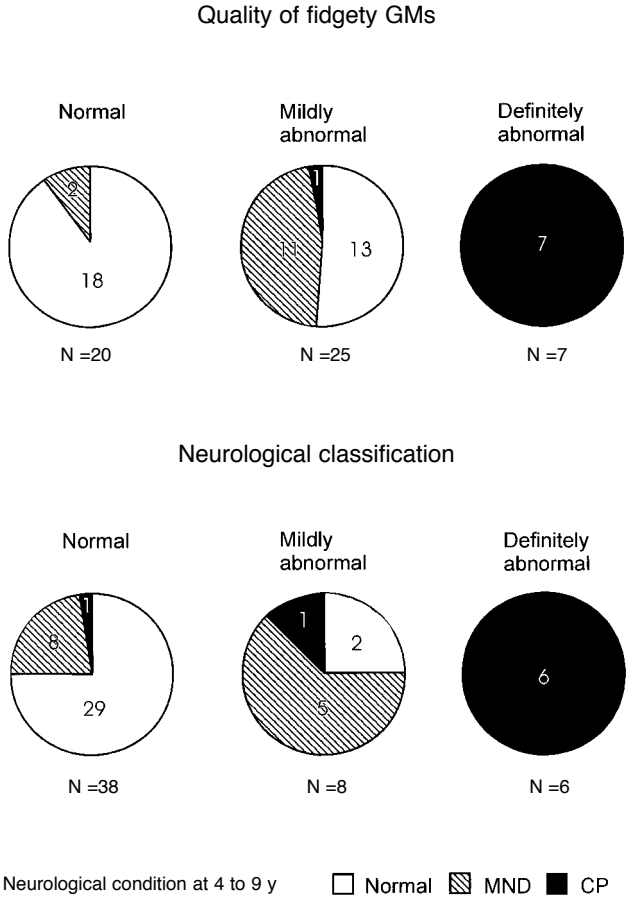

Figure 2: *Neuromotor behaviour at fidgety-GM age and neurological condition at 4 to 9 years.*

with a mild hypertonia or an unstable muscle tone 4.0±2.2; $t=5.17$, $P<0.001$).

The quality of GMs was related to neurological outcome (Fig. 1). The prediction of neurological development based on GM quality during the preterm GM phase was relatively poor: one of four infants with definitely abnormal GMs and three of 13 infants with mildly abnormal GMs developed CP. Only one infant had normal GMs in the preterm period. This child did, however, develop CP due to a severe streptococcal meningitis shortly before term age. The best prediction of neurological outcome from GM quality during a single GM phase was from GM quality during fidgety GM age (Figs. 1 and 2). All seven infants with definitely abnormal GMs at fidgety age, denoting the total absence of the elegant fidgety movements, developed CP. In the group of 25 children with mildly abnormal GMs at fidgety age, one child developed a mild hemiplegia, and 13 MND. In the group of 20 children with normal fidgety movements, only two children developed MND and none CP. The difference in prevalence of MND between children with normal and mildly abnormal GMs at fidgety age was statistically significant ($\chi^2=6.73$, $P<0.01$). In those children in whom mildly abnormal GMs at fidgety age had been preceded by definitely abnormal GMs at writhing age, neurological outcome was somewhat worse than in those children in whom mildly abnormal fidgety GMs had been preceded by mildly abnormal GMs at writhing age (difference in neurological normal outcome: Fisher $P=0.09$, *ns*).

Table VI illustrates the predictive power of GM assessment and the infant neurological examination at two ages (writhing-GM phase and fidgety-GM phase) for the development of CP and MND. Prediction of CP was good with both instruments, with an accuracy of 90% at writhing age and 96 to 98% at fidgety age. Both methods had an excellent specificity for the prediction of CP, i.e. definite abnormalities at fidgety age were associated with the development of CP. The sensitivity for both methods differed slightly, with a small advantage for GM assessment (Fig. 2). For both methods, accuracy in predicting the development of MND was considerably lower than accuracy in predicting CP (Table VI). GM assessment had a high sensitivity for predicting the development of MND, but a rather low specificity, indicating that normal GMs predicted a normal neurological outcome very well, but mildly abnormal GMs at fidgety age were only followed by the development of MND in about half of the cases. For the neurological assessment the reverse was true: a low sensitivity and a high specificity, i.e. few false positives and a considerable number of false negatives.

Neonatal ultrasound data of the brain were only available in the 24 high-risk children. Eight children had normal ultrasounds, two of them were neurologically normal at follow-up, four had MND, and two CP. In the group of 10 children with mildly abnormal ultrasound findings, four were neurologically normal at school age, five developed MND, and one CP. None of the six children with definitely abnormal ultrasounds was neurologically normal at follow-up, one had MND, and five CP. This means that accuracy in predicting the development of CP on the basis of definitely

Table IV: Changes in GM quality

Period	*Nr of infants with multiple recordings*	*Nr of infants in whom GM quality changed*
Within-GM phase		
Preterm GMs (<38 wk)	3	0
Writhing GMs (38–47 wk)	35	4
Fidgety GMs (>47 wk)	48	1
Between-GM phases		
Preterm to writhing	18	4
Writhing to fidgety	52	13

Differences in the frequency of changes between the between- and within-GM phases: preterm to writhing versus within-GM phases, no significant differences; writhing to fidgety versus within-GM phases, no significant differences with preterm and writhing periods, and a significant difference with fidgety period, $\chi^2=9.07$, $P<0.01$.

Table V: Number of children with neurological conditions at 4 to 9 years

Neurological condition at 4 to 9 years	*Low-risk group*	*High-risk groups*	
		Term-asphyxia	*Preterm*
	(N=28)	*(N=6)*	*(N=18)*
Normal	25	2	4
MND	3	1	9
Choreiform dyskinesia	1	0	0
Mildly abnormal muscle tone[a]	0	1[b]+B	2 (1[c],1[d]+B)
Mildly abnormal muscle tone and coordination problems	1[b]	0	5 (2[c],1[b],2[d])
Mildly abnormal muscle tone and problems in coordination and FMA	1[c]	0	2[b]
Cerebral palsy	0	3	5
Spastic hemiplegia	0	1	2
Spastic diplegia	0	1	1
Spastic tetraplegia	0	1	2

[a] mildly abnormal muscle-tone regulation: number of children with specific types of mild tone regulation between brackets:
[b] unstable muscle tone
[c] mild hypotonia, changing from mild hypotonia to mild hypertonia
[d] mild hypertonia.
B, presence of Babinski sign at the foot-sole response.
FMA, fine manipulative abilities.

abnormal ultrasound findings is good (83%), but is lower than that when based on the assessment of the quality of GMs. The lower accuracy of the neonatal ultrasound findings can be attributed to a relatively low sensitivity (62%), which points to the presence of false negatives. Analysis of outcome on the basis of both ultrasound findings and GM assessment at fidgety age indicated that the quality of the GMs contributed more to prediction than the ultrasound findings. The seven children with definitely abnormal movements at fidgety age all developed CP, while their ultrasound findings were classified as follows: normal in two, mildly abnormal in one, and definitely abnormal in four.

GM QUALITY AND BEHAVIOUR AT FOLLOW-UP

The analysis of the relation between GM quality and behavioural development was restricted to the children without CP. The quality of GMs at preterm age was not related to behavioural outcome, and that at writhing age to a minor extent only. However, GM quality at fidgety age showed a significant correlation with behaviour at school age. Due to the exclusion of children with CP from the behavioural analysis, only the effect on behavioural development of normal and mildly abnormal GMs at fidgety age could be analysed.

The Total Score of the CBCL did not differ for children with normal and mildly abnormal GMs at fidgety age. Yet children with mildly abnormal GMs at fidgety age ($N=24$) had significantly higher scores on two of the subscores of the CBCL than children with normal fidgety GMs ($N=20$; Fig. 3). The difference was present in the Externalizing Score (median values for the group with normal fidgety GMs 4.5 and for those with mildly abnormal fidgety GMs 14; Mann–Whitney, P=0.04) and in Aggressive Behaviour (median values 4.5 and 11.5, respectively; Mann–Whitney, P=0.03). GM quality did not show a significant relation with the Attention Problem score of the CBCL.

Both the GPPQ and the DSM questionnaire on ADHD did, however, point to a significant correlation between GM quality at fidgety age and the development of attention problems. The GPPQ showed that children with normal fidgety GMs and those with mildly abnormal fidgety movements differed selectively on the item 'Distractible Behaviour'. The parents of the group of children with normal fidgety GMs rated 55% of children as not easily distracted, 20% as rather easily distracted, and 25% as very easily distracted. For the group of children with mildly abnormal fidgety GMs, the figures were 17%, 37%, and 46%, respectively ($\chi^2=7.14$, $df=2$, P=0.03). The parents of children with mildly abnormal fidgety GMs also rated their children significantly more often on the DSM questionnaire as suffering from 'inattention', 'hyperactivity', and ADHD than the parents of children with normal fidgety GMs (Fig. 4).

Due to behavioural problems having a multifactorial origin, we tested the above-mentioned correlations between GM quality at fidgety age and behaviour with multivariate statistics. We entered the following variables as confounders into the analysis: social class, age at follow-up, sex, gestational age at birth, birthweight, findings on the neonatal

Table VI: Predictive power (%) of GM assessment and the infant neurological examination for the development of neurological dysfunction and ADHD at school age

	Assessment at writhing-GM phase		*Assessment at fidgety-GM phase*	
	GM	*Neurological*	*GM*	*Neurological*
Prediction of CP	(DA)	(DA)	(DA)	(DA)
Sensitivity	100	75	88	75
Specificity	89	93	100	100
Accuracy	90	90	98	96
Positive predictive value	62	67	100	100
Negative predictive value	100	95	98	96
Prediction of MND in children without CP	(DA + MA)	(DA + MA)	(MA)	(DA + MA)
Sensitivity	85	38	85	38
Specificity	48	90	58	94
Accuracy	59	75	66	77
Positive predictive value	41	62	46	71
Negative predictive value	82	78	90	78
Prediction of ADHD (DSM questionnaire) in children without CP	(DA + MA)	(DA + MA)	(MA)	(DA + MA)
Sensitivity	86	7	79	7
Specificity	50	77	57	80
Accuracy	61	55	64	57
Positive predictive value	44	12	46	46
Negative predictive value	88	52	85	35

Sensitivity, true positives/(true positives + false negatives).
Specificity, true negatives/(true negatives + false positives).
Accuracy, (true positives + true negatives)/all subjects.
Positive predictive value, true positives/all positives.
Negative predictive value, true negatives/all negatives.
DA, definitely abnormal; MA, mildly abnormal.

ultrasound scans of the brain, and intercurrent disorders. The analyses showed that all behavioural outcomes depended on the combination of the quality of GMs at fidgety age and social class. This was true for the multiple regression analysis of the Externalizing Score and the Aggressive Behaviour of the CBCL, which showed that a higher score on these behavioural items was significantly related (r^2=0.40 and 0.41, respectively, P<0.05) to mildly abnormal fidgety GMs (P=0.04 and 0.02) and a higher social class (P=0.03 and 0.04). Similarly, logistic regression analysis demonstrated a significant contribution of mildly abnormal fidgety GMs and a higher social class to the development of attention problems as scored on the GPPQ and DSM questionnaire. For example, the odds ratio for mildly abnormal GMs for the development of ADHD as scored on the DSM questionnaire was 6.88 (95% confidence intervals 1.39 to 33.97).

The accuracy for predicting the development of attention problems from GM assessment was similar to that of predicting MND from GM assessment (around 60 to 65%; Table VI). GM assessment resulted in few false negatives, but a substantial number of false positives in the prediction of attention problems. The predictive power of the infant neurological examination for attention problems was low, which could be attributed to the low sensitivity of the test. Very few children developing attention problems showed abnormalities at the infant neurological examination.

Finally we assessed comorbidity of MND and ADHD as scored on the DSM questionnaire (Fig. 5). Only three children showed both MND and ADHD. All three had had mildly abnormal GMs at fidgety age. Most children with problems had either MND or ADHD. Children with neither MND nor ADHD tended to be in the group of children with normal fidgety GMs (75%) rather than in the group of children with mildly abnormal GMs (21%; χ^2=12.9, P<0.0001).

Discussion

PERSISTENCY AND CHANGES IN NEUROBEHAVIOURAL DEVELOPMENT

The present study indicates that the quality of GMs, and in particular the quality of GMs at fidgety age, is related to neurological and behavioural condition at school age.

Before commenting on the significance of our results, we wish to make some methodological remarks. The present study deals with two non-random samples of children. The first group consisted of healthy children born at term considered to be at low risk for developmental problems. None of them developed CP, 11% showed MND, and 25% were rated as having ADHD on the parental DSM questionnaire. This prevalence of MND and ADHD are comparable to those found in general populations of school-age children (Gillberg and Rasmussen 1982, Hadders-Algra et al. 1988a, Verhulst and Althaus 1988), suggesting that our group of healthy term children was a representative group of healthy term children. The high-risk group was either term children with severe perinatal asphyxia or preterm infants, who were treated for several weeks in the University Hospital. Preterm children, who stay for several weeks in our hospital, constitute a negative sample of preterm infants, as the University Hospital is a provider of tertiary care. This could explain why the preterm infants of the present study seldom showed normal GMs. An alternative explanation for the high rate of mildly abnormal

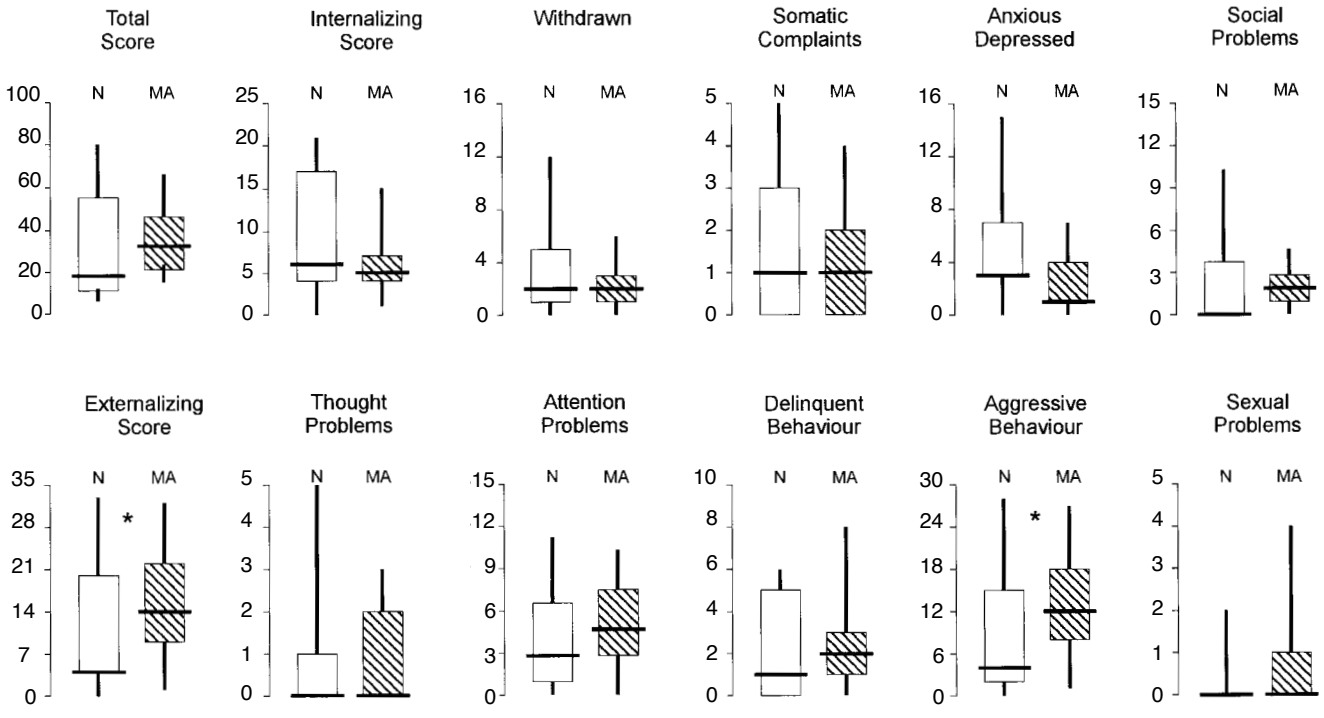

Figure 3: *Quality of fidgety GMs and CBCL scores. Data are presented by ranges (vertical bars), interquartile ranges (boxes), and median values (horizontal bars). N, normal fidgety GMs (N=20); MA, mildly abnormal fidgety GMs (N=24).*
** Mann–Whitney, P≤0.05.*

GMs in the preterm infants, in accordance with other findings, could be that preterm infants often have minor degrees of brain dysfunction. Indeed, Kakebeeke et al. (1998) that both high- and low-risk preterm infants show GMs of an inferior quality in comparison to those of term neonates. Furthermore, recent findings in two studies on postural control, have indicated that preterm children, including those with perfectly normal ultrasound scans of the brain, have problems with the adaptation of postural adjustments to task-specific conditions (Hadders-Algra et al. 1999, Van der Fits et al. 1999). Long-term follow-up studies of preterm infants have also indicated that about half of these children have learning and/or attention problems (Ornstein et al. 1991, Saigal et al. 1991, Hall et al. 1995).

Another methodological issue which deserves attention is that the low-risk children were significantly older at follow-up than the high-risk children. The prevalence of MND is known to increase with age before puberty (Hadders-Algra et al. 1988a, Lunsing et al. 1992, Hadders-Algra and Touwen 1999). This means that in the younger high-risk group the signs of MND were relatively underrepresented compared with those in the older low-risk group. This might have occluded a part of the differences between the low- and high-risk groups and between the groups with normal, mildly abnormal, and definitely abnormal GMs. Notwithstanding a partial occlusion, clear differences in neurological outcome in the various groups were found.

The present study indicates that considerable changes can occur in GM quality. Movement quality can deteriorate (usually before term age) and it can improve (in general during the postterm ages), and thus previous authors have emphasized the need for developmental trajectories of GM quality for the prediction of developmental outcome (Ferrari et al. 1990, Prechtl 1990, Prechtl et al. 1993, Bos 1997). The present data suggest that the changes in GM quality coincide with the transitional ages during the form of normal GM changes, i.e. between 36 and 38 weeks' PMA and between 46 and 48 weeks' PMA (Hadders-Algra et al. 1997). If GMs repeatedly show a definitely abnormal quality despite the processes of neural transformation, this might imply a basic deficit in motor coordination. This, in turn, could explain why children who consistently show definitely abnormal GMs throughout the first postnatal months are at high risk of developing CP.

GM quality at fidgety age predicted outcome best. The prediction for neurological outcome became a little stronger when GM quality at writhing age was known as well. Similar 'writhing' information did not enhance the prediction of behavioural problems. GM quality during preterm age did not have an (additional) prognostic significance. The strong predictive power of definitely abnormal GMs at fidgety age for the development of CP has been reported before (Hadders-Algra et al. 1997, Prechtl et al. 1997). The present study indicates that mildly abnormal GMs at fidgety age also have a prognostic significance, pointing to an increased risk for the development of MND, ADHD, and boisterous, disobedient behaviour. The data revealed that prediction of MND and behavioural problems was weaker than the prediction of CP, probably because environmental factors play a more important role in the development of minor forms of brain dysfunction than in the development of CP (Hadders-Algra et al. 1988a, b). Remarkably, the development of attention problems and aggressive behaviour was associated with a higher social class. This is an unusual finding, which does not agree with reports of others (Rutter 1982, Biederman et al. 1995), nor with previous results of our own (Hadders-Algra et al. 1988b). It is conceivable that such behavioural problems are due to recent changes in Dutch society: the number of working mothers has increased considerably during recent years, particularly in groups with higher socioeconomic status. However, facilities, such as day nurseries, have remained scarce, resulting in high levels of organizational stress for

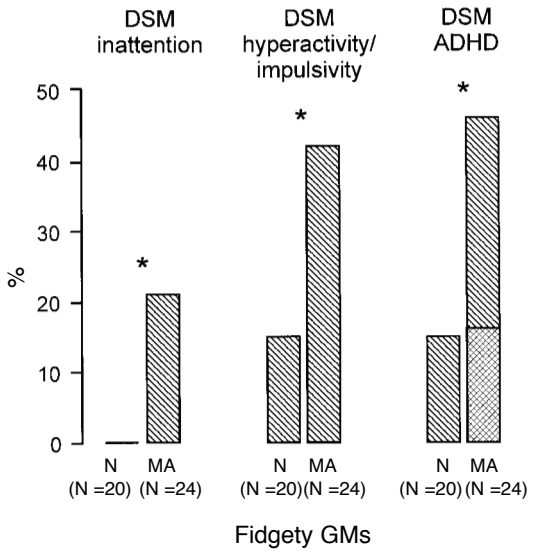

Figure 4: *Quality of fidgety GMs and ADHD problems as scored on the DSM questionnaire. * P<0.05 on Fisher (inattention) or χ^2 (hyperactivity and ADHD). N, normal; MA, mildly abnormal. Hatched areas indicate presence of either inattention or hyperactivity. Cross-hatched areas indicate presence of inattention and hyperactivity.*

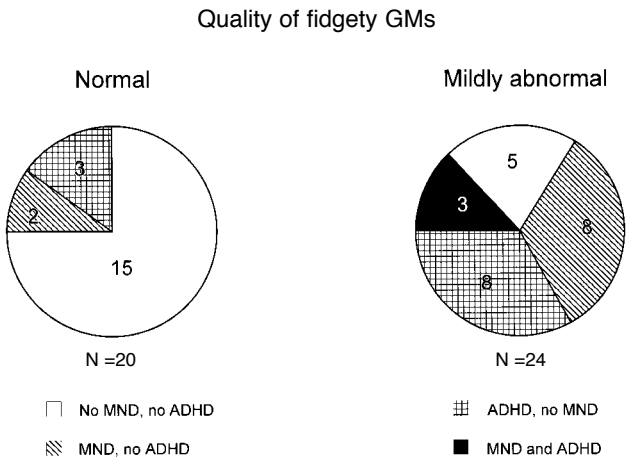

Figure 5: *Quality of fidgety GMs and presence of MND and ADHD (DSM questionnaire) at 4 to 9 years.*

working Dutch mothers and their families.

Abnormal findings at the infant neurological examination also predicted neurological outcome well, but the neurological examination occasionally missed an infant who developed CP. Cioni et al. (1997a, b) reported that this happens especially in preterm infants. In contrast to GM assessment, the neurological findings did not predict behavioural development. This might imply that GM assessment is a more sensitive instrument than the classical infant neurological examination, as its prediction not only covers the neurological domain, but also the behavioural area, which is governed by multiple subtle neural mechanisms.

The presence of mildly abnormal GMs at fidgety age was related to the development of MND. Mildly abnormal GMs are characterized by an absence of movement fluency and a deficient muscle coordination (Hadders-Algra et al. 1997). In this respect it is interesting to note that the children with MND were characterized by a similar neurological profile. Their main motor dysfunctions consisted of coordination problems and mild abnormalities in muscle-tone regulation, the latter being associated with a non-fluent (usually stiff) motility of legs and trunk. This indicates that the neurological condition was relatively stable in a substantial number of children – and perhaps such a stability of neurological condition occurs more often than previously thought. Such a stability in neurological function is not at variance with developmental changes in the nervous system. It means that MNDs remain present, notwithstanding the maturational changes in the brain. The developmental changes occur in the way the dysfunctions are expressed. For instance, at an early age the minor dysfunctions can be expressed as mildly abnormal GMs and at school age as coordination problems.

The comparison of the EMGs of the mildly abnormal GMs with neurophysiological data of animal experiments suggests that the mildly abnormal GMs are related to dysfunctions of the monoaminergic (serotonergic and dopaminergic) systems (Kiehn and Kjaerulff 1996, Kiehn et al. 1996, Hadders-Algra et al. 1997). This could explain the relation found in the present study between mildly abnormal GMs on the one hand, and attention problems and boisterous, disobedient behaviour on the other hand. ADHD is associated with dopaminergic dysfunctions in the frontostriatal circuitries (Lou 1996, Castellanos 1997), whereas serotonergic dysfunction is considered to play a role in the genesis of aggressive behaviour (Kavoussi et al. 1997). Part of the monoaminergic dysfunctions could be due to mild chronic hypoxia in early life, as animal experiments indicated that chronic or repetitive mild hypoxic insults can result in long-term changes in the striatal dopaminergic system (Gross et al. 1993, Mallard et al. 1995).

CLINICAL IMPLICATIONS

The present study with its heterogeneous study groups suggests that the quality of GMs at fidgety age is a sensitive predictor for the child's neurological and behavioural development. Notwithstanding the fact that further research in larger random populations is required to determine the exact risks related to the presence of definitely and mildly abnormal GMs at fidgety age, we now propose that the assessment of fidgety GMs is included in the standard assessment of young infants, the primary reason being, in our opinion, that the presence of definitely abnormal GMs at fidgety age is an indication for physiotherapeutic intervention. We do not think that the intervention will prevent the development of CP, but we assume that an early intervention improves the child's later functional abilities. The clinical implications of the information that a child shows mildly abnormal GMs at fidgety age are less clear. We suggest that mildly abnormal GMs point to the presence of a non-optimally wired brain, which puts the infant at risk for the development of MND, ADHD, and aggressive behaviour, and whether the latter problems do develop, is mainly determined by the presence of unfavourable conditions. Therefore, it is our strategy to tell the parents of an infant with mildly abnormal GMs at fidgety age, that their infant has a specific 'temperamental make up', which makes it less tolerant of environmental adversities.

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