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Typical general movements at 2 to 4 months: Movement complexity, fidgety movements, and their associations with risk factors and SINDA scores

Ying-Chin Wu^{a,b}, Elisabeth J.M. Straathof^a, Kirsten R. Heineman^{a,c}, Mijna Hadders-Algra^{a,*}

^a University of Groningen, University Medical Center Groningen, Department of Paediatrics, Division of Developmental Neurology, Groningen, the Netherlands

^b Department of Physical Therapy, Chung Shan Medical University, Taichung, Taiwan

^c SEIN, Stichting Epilepsie Instellingen Nederland, Zwolle, the Netherlands

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ABSTRACT

Background: Movement complexity and the presence of fidgety movements (FMs) during general movements (GMs) both reflect aspects of neurological integrity in early infancy.

Aim: To assess interrelations between the degree of movement complexity and characteristics of FMs during typical GMs and to investigate associations between mildly impaired GMs and risk factors and neurodevelopmental condition.

Study design: Observational cohort study.

Subjects: 283 infants (25 born preterm) at 2–4 months corrected age, representative of the general Dutch population.

Outcome measures: GMs were classified in terms of GM-complexity (normal or mildly abnormal (MA)) and FMs (clearly present, sporadic, or exaggerated). Concurrent neurological, developmental and socio-emotional status were measured with the Standardized Infant NeuroDevelopmental Assessment (SINDA).

Results: Infants with MA GM-complexity had a higher risk of having sporadic FMs and exaggerated FMs. Perinatal complications were not associated with mildly impaired GMs. MA GM-complexity was associated with advanced maternal age (adjusted OR = 2.29 [1.11, 4.76]) and having a non-native Dutch mother (adjusted OR = 2.93 [1.29, 6.64]). It was also associated with atypical neurological (OR = 7.62 [3.51, 16.54]) and developmental scores (OR = 2.38 [1.16, 4.88]). Sporadic and exaggerated FMs were associated with low-to-middle maternal education (adjusted OR = 2.88, [1.45, 5.72]) and having a non-native Dutch father (adjusted OR = 7.16 [1.41, 36.32]), respectively. However, neither sporadic nor exaggerated FMs were associated with the SINDA outcomes.

Conclusions: GM-complexity and FMs are two interrelated but different aspects of GMs. Mild impairments in GM-complexity and FMs share a non-optimal socio-economic background as risk factor, but only MA GM-complexity is associated with a concurrent non-optimal neurodevelopmental condition.

1. Introduction

General movements (GMs) are spontaneous movements involving all parts of body in the fetus and infant before the emergence of goal-directed movements. The quality of GMs reflects the quality of neurological function in early life and typical GMs are characterized by complexity and variation and the presence of age-specific properties. Before near-term, during the fetal or preterm phase, GMs include large trunk movements and pelvic tilts. Around 36–38 weeks postmenstrual age, when the writhing phase starts, trunk movements decrease and GMs

become forceful. During the fidgety phase at 2 to 5 months post-term, the forceful movements are replaced by tiny, elegant and rhythmic movements, so-called fidgety movements (FMs) [1,2].

Assessment of GMs allows early detection of infants at risk of cerebral palsy (CP) [3]. The predictive power is particularly high when it is performed during the fidgety phase [4]. There are two variants available to assess the quality of GMs in the fidgety phase, which essentially assess the same constructs – movement repertoire and FMs, but they also have slight differences. Precht's method [1] focuses primarily on the features of FMs and classifies the temporal organization of FMs into

Abbreviations: CA, corrected age; CP, cerebral palsy; DA, definitely abnormal; FM, fidgety movement; GM, general movement; GMA, general movement assessments; IMP, Infant Motor Profile; MA, mildly abnormal; OR, odds ratio; SINDA, Standardized Infant NeuroDevelopmental Assessment

* Corresponding author at: Division of Developmental Neurology, Department of Paediatrics, University Medical Center Groningen, Hanzeplein 1, 9713 GZ Groningen, the Netherlands.

E-mail address: m-hadders-algra@umcg.nl (M. Hadders-Algra).

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continual, intermittent, sporadic and absent. The latter two are considered abnormal. FMs are also labelled abnormal when they have an exaggerated appearance [1]. In addition, the concurrent movement repertoire was evaluated in some studies [5–7]. Hadders-Algra's classification primarily [8] pays attention to the movement repertoire in terms of movement complexity and variation (in short: complexity), which is classified into four categories: normal-optimal, normal-sub-optimal, mildly abnormal (MA) and definitely abnormal (DA). At fidgety GM-age, Hadders-Algra also pays attention to the features of FMs [9,10]. The presence of atypical GMs in the clinically relevant forms, i.e., DA GM-complexity or absent FMs, is strongly associated with premature birth [11,12] and perinatal brain lesions [13,14], and predicts cerebral palsy [2,4]. Note that especially the presence of the combination of DA GM-complexity and absent FMs is associated with a very high risk of CP [9].

GM-complexity and FMs are different parameters of GM-quality that are presumably based on a different neurobiological substrate [2]. This is not only indicated by the fact that GM-complexity is characteristic for GMs from early fetal age onwards and FMs are only observed in the last phase of GMs (between 2 and 5 months post-term), but also by other observations. First, GM-complexity has been noted to be relatively stable within the fidgety phase [15,16]; however, FMs in the fidgety phase are dependent on the infant's age, with less fidgety movements being observed in the age margins of the phase [17]. Second, GM-complexity was associated with cognition in infancy [11] and at school age [6,7,15,18]. In contrast, various studies indicated that absent FMs did not predict cognitive outcome [6,18,19]. Only Spittle et al. [20] and Datta et al. [21] reported that preterm infants with absent FMs had lower cognitive scores at 2 and 4 years. However, this association disappeared when children with CP were excluded [21]. Third, a lower socio-economic state was associated with the presence of MA and DA GM-complexity [22] but not with absent FMs [21]. Fourth, our previous study in infants representative of the general Dutch population revealed that the prevalence of DA GM-complexity and the prevalence of absent FMs were both 3%, but only 0.3% of the population had both impairments. Moreover, maternal smoking increased the risk of DA GM-complexity, whereas the absence of FMs was not associated with perinatal risk [23].

Realizing that GM-complexity and FMs are two different but inter-related aspects of GMs, we embarked on this study that addresses GM-complexity and FMs in infants having GMs within the typical spectrum (non-DA GM-complexity and present FMs). Three specific questions are addressed: 1) are GM-complexity and FMs interrelated during GMs within the typical spectrum? 2) what are the risk factors of MA GM-complexity and mildly impaired FMs? and 3) are mild impairments in GM-complexity and FMs associated with concurrent neurodevelopmental condition measured by the Standardized Infant NeuroDevelopmental Assessment (SINDA; [24,25])? We hypothesized that 1) infants who show MA GM-complexity are more likely to have sporadic and exaggerated FMs; 2) prenatal and perinatal complications, including preterm birth, are associated with MA GM-complexity and sporadic and exaggerated FMs, whereas a lower socio-economic state [22] is associated only with MA GM-complexity; and 3) infants with MA GM-complexity, sporadic or exaggerated FMs have lower neurological and developmental SINDA scores.

2. Methods

2.1. Participants

The study group was based on the IMP-SINDA project. This project aimed to collect norm data of two assessment tools: the Infant Motor Profile (IMP) [26] and the SINDA [24,25] in a sample representative of the general Dutch population in terms of maternal education and ethnicity. The age range of the IMP is 3 to 18 months, that of the SINDA 2 to 12 months, hence the age range of the IMP-SINDA project was 2 to 18 months. One hundred infants were included per month of age,

fulfilling the following inclusion criteria: age 2–18 months corrected age (CA), living in the northern part of the Netherlands and having caregivers with sufficient understanding of the Dutch language. Infants were excluded only when they were too ill to be assessed (e.g. severe congenital cardiac disorder with the need of oxygen support). The recruitment was conducted via well-baby clinics and advertisements between January 2017 and March 2019. All parents gave written informed consent and background information of the infants was obtained by a standardized questionnaire. If the questionnaire revealed complications, e.g. premature birth or admission to the neonatal ward, medical records were consulted. The project was approved by the Medical Ethical Committee of the University Medical Center Groningen (METc 2016/294) and registered in the Dutch trial register (NL58069.042.16).

In the youngest infants the assessment battery included a video recording of spontaneous movements in supine [23]. This allowed for general movements assessment (GMA) in the 300 infants aged 2, 3 and 4 months, composing the GM-study sample. For the current project infants were only eligible when their GM-quality fell within the typical spectrum. This means that they were excluded if they showed DA GM-complexity or absent FMs. The findings in the infants excluded from the present study ($n = 17$) have been reported in Wu et al. 2020 [23]. The basic characteristics of the final sample (258 term-born and 25 preterm infants, of whom 6 were born < 32 weeks) are presented in Table 1.

2.2. Procedure

Infants were assessed at home, at well-baby clinics or at the baby-lab of Developmental Neurology, depending on the parents' preference. During the assessment, the infants wore only a bodysuit and diaper. The IMP-SINDA assessment started with a recording of infant's spontaneous movements in an awake state in supine for at least 3 min, as part of IMP assessment. This part of the assessment was used for GMA. SINDA was performed by a team of trained assessors, under the supervision of two experts (MHA and KRH). Supervision consisted of a combination of live and video supervision.

GMA was performed offline from the video recording by MHA, who has applied GMA for more than 25 years. She was masked for the background of the infants. As MHA was one of the supervisors of SINDA, the scoring of GMA was performed with a three-to-six-month delay to keep her blinded from the SINDA results.

2.3. GMA

GMA consisted of the evaluation of GM-complexity and FMs. GM-complexity was classified as normal-optimal (abundant complexity, variation and fluency), normal-suboptimal (sufficient complexity and variation, no fluency) and MA (insufficient complexity and variation, no fluency) [8]. Normal-optimal and normal-suboptimal GM-complexity do not differ in predicting neurodevelopmental outcome [27]. They were therefore pooled into the category of “normal” GM-complexity. MA GM-complexity, as a single sign, has a limited clinical value, it represents the lower end of typical brain function [2].

FMs were scored in terms of the temporal organization and quality. The classifications of temporal organization were: continual (frequent occurrence in the whole body with very short pauses of 1–2 s), intermittent (occurrence in the whole body with prolonged pauses of 1–10 s) and sporadic (isolated occurrence in a few body parts with long pauses up to 1 min; [1]). As infants with continual or intermittent FMs are likely to develop typically [1], we pooled these two categories into one labelled “clearly present”. The significance of sporadic FMs is less clear; it did not predict CP [9], but it has been reported to be associated with a lower gross motor score within the normal range [5]. The quality of FMs was dichotomized into normal or exaggerated (exaggerated in amplitude, speed and jerkiness). The clinical value of exaggerated fidgety movements is also low when occurring as a single sign [28].

Table 1
Basic characteristics of participants.

	Study cohort (<i>n</i> = 283)	
	<i>n</i> of data	Median (range) or <i>n</i> (%)
Prenatal and perinatal characteristics		
Pre-pregnancy maternal BMI in kg/m ²	281	24.1 (17.4–43.2)
Overweight or obesity (BMI ≥ 25 kg/m ²)	281	122 (43)
Assisted reproduction	280	22 (8)
Maternal smoking	282	33 (12)
Substance exposure (alcohol or drugs)	282	5 (2)
Maternal medication ^a	282	32 (11)
Maternal hypertension	282	35 (12)
Maternal diabetes	282	24 (9)
Maternal thyroid disease	282	9 (3)
Instrumental delivery	283	58 (21)
Sex: Male	283	152 (54)
Twin	283	10 (4)
Birthweight in grams	283	3370 (1120–4875)
Small for gestational age ^b	283	42 (15)
Gestational age in weeks	283	39.4 (27.3–42.1)
Preterm birth (< 37 weeks)	283	25 (9)
In infants born preterm		
Neonatal intensive care admission	25	6 (24)
5-min Apgar score < 7	25	3 (12)
Cranial ultrasound findings		
No indication for ultrasound or no abnormality	25	20 (80)
Periventricular flaring	25	3 (12)
Intraventricular haemorrhage: grade I	25	2 (8)
Infection/sepsis	25	4 (16)
Meconium in amniotic fluid	281	35 (13)
Hyperbilirubinemia requiring phototherapy	282	17 (6)
Socio-economic characteristics		
Maternal age in years	283	30 (16–44)
Advanced maternal age (age ≥ 35 years)	283	46 (16)
Paternal age in years	277	32 (21–68)
Advanced paternal age (age ≥ 40 years)	277	35 (13)
Maternal educational level: high ^c	283	115 (41)
Paternal educational level: high ^c	273	111 (41)
Maternal ethnicity: non-native Dutch	283	31 (11)
Paternal ethnicity: non-native Dutch	278	26 (9)
Assessment age in weeks ^d	283	12 (6–20)

BMI = body mass index.

^a Maternal medication indicates the use of at least one of the following: insulin, antihypertensive medication, thyroid stimulating medication, antidepressants/antipsychotics/benzodiazepines, anti-epileptic medication.

^b Small for gestational age: birth weight for gestational age < 10th percentile of Dutch growth curves.

^c High educational level: vocational college and university.

^d Corrected age is used in all infants, calculated from the expected birth date and assessment date, rounded down to weeks.

2.4. SINDA

SINDA is a screening tool to assess neurodevelopment in infants aged 6 weeks to 12 months [24,25]. It consists of three scales: a neurological, developmental and socio-emotional scale. SINDA's neurological scale has 28 items assessing five domains: spontaneous movements, cranial nerve function, motor reactions to postural stimulation, muscle tone and reflexes. The developmental scale comprises 15 age-specific items per month, covering cognition, communication, fine and gross motor development. Items in the neurological and developmental scales are scored as pass (1 point) or fail (0), resulting in a neurological and a developmental score. Both scores are independent of infant's age. A neurological score of ≤21 and a developmental score of ≤7 are atypical. The socio-emotional scale assesses four behaviours: interaction, emotionality, self-regulation and reactivity. Each behaviour is classified as typical or atypical. The psychometric properties of SINDA have recently been reported in groups of infants at risk of a

neurodevelopmental or neurological disorder, showing a high reliability (0.78–0.97) and satisfactory item discrimination and predictive validity [24,25]. Atypical neurological scores predict atypical developmental outcome (sensitivity 83–89%, specificity 94–96%) and CP (sensitivity 100%, specificity 81%) at 24 months or older [24,25], atypical developmental scores predict intellectual disability (sensitivity 77%, specificity 92%) and atypical emotionality and self-regulation are associated with behavioural or emotional disorder (odds ratio = 12.99 and 21.11 respectively) [25].

2.5. Statistics

The relation of GM-complexity and FMs was tested by logistic regression analyses. Risk factors of mildly impaired GMs, i.e., MA GM-complexity, sporadic or exaggerated FMs, were explored by two-step regression analyses. The associations of background characteristics and the presence of mildly impaired GMs were investigated first with univariable regression analyses. Characteristics showing a significant association in the univariable analysis were then entered into a multivariable regression analysis to reveal the determinants of mildly impaired GMs. The concurrent association between the GMs and SINDA was examined by Mann-Whitney *U* test for the SINDA scale scores and logistic regression analysis for the presence of an atypical score or behaviour. As the temporal organization of FMs is age-dependent, the age effect was accounted for in two ways: 1) in the regression models of the FMs by adding age and its quadratic function, 2) by repeating the analysis in the subgroup of infants at the age of 9 to 15 weeks, when FMs peak. The strength of associations was presented as odds ratio (OR) and its 95% confidence interval. A *p* < 0.05 was considered to be statistically significant. All analyses were conducted with IBM SPSS Statistics 23 (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. GM-complexity and FMs

Of the total 283 participants, 52 (18%) infants showed MA GM-complexity. FMs were sporadic in 60 (21%) infants and exaggerated (while being clearly present in temporal organization) in 7 (2%). Twenty-four (8%) infants showed MA GM-complexity in combination with mildly impaired FMs (sporadic or exaggerated). GM-complexity was associated with the temporal organization and the quality of FMs: infants with MA GM-complexity had a higher risk of having sporadic FMs (in the entire sample: adjusted OR = 2.81 [1.39, 5.68]; in infants aged 9–15 weeks: OR = 6.36 [2.47, 16.33]) and exaggerated FMs (OR = 40.29 [4.67, 347.20]).

3.2. Risk factors of abnormal GMs

In the univariable analyses MA GM-complexity was significantly associated with advanced maternal age (OR = 2.62 [1.29, 5.32]) and having a non-native Dutch mother (OR = 3.35 [1.51, 7.43]) (Table 2). Multivariable analysis suggested that both factors continued to be associated with MA GM-complexity: advanced maternal age (adjusted OR = 2.29 [1.11, 4.76]) and non-native Dutch mother (adjusted OR = 2.93 [1.29, 6.64]).

After controlling for infant age, sporadic FMs were only associated with low-to-middle maternal educational level (in all infants: adjusted OR = 2.88, [1.45, 5.72], Table 2; in infants aged 9–15 weeks: OR = 4.60 [1.51, 14.00]). In the univariable analyses exaggerated FMs were associated with meconium-stained amniotic fluid (OR = 5.45 [1.16, 25.74]) and having a non-native Dutch father (OR = 8.69 [1.80, 42.06], Table 2). In the multivariable analysis only the association with a non-native Dutch father remained significant (adjusted OR = 7.16 [1.41, 36.32]).

Table 2
Associations of basic characteristics with mildly impaired general movements (GMs).

	Mild impairments at GM assessment		
	MA GM-complexity (<i>n</i> = 52)	Sporadic FMs (<i>n</i> = 60) ^a	Exaggerated FMs (<i>n</i> = 7) ^a
Univariable logistic regression			
Prenatal and perinatal characteristics			
Maternal overweight or obesity	0.95 [0.52, 1.74]	0.90 [0.49, 1.64]	0.97 [0.21, 4.42]
Maternal smoking	0.98 [0.38, 2.51]	1.44 [0.61, 3.38]	._b
Maternal medication	1.88 [0.82, 4.35]	0.58 [0.19, 1.74]	._b
Maternal hypertension	1.37 [0.58, 3.21]	0.94 [0.38, 2.32]	._b
Maternal diabetes	1.54 [0.58, 4.08]	1.06 [0.37, 3.01]	._b
Instrumental delivery	1.05 [0.50, 2.20]	1.06 [0.52, 2.16]	._b
Sex: male	0.90 [0.49, 1.65]	1.56 [0.87, 2.82]	0.96 [0.21, 4.37]
Twin	3.13 [0.85, 11.50]	0.34 [0.04, 2.98]	._b
Small for gestational age	1.26 [0.56, 2.82]	0.49 [0.18, 1.33]	0.83 [0.10, 7.13]
Prematurity	1.84 [0.73, 4.67]	1.04 [0.38, 2.81]	._b
5-min Apgar score < 7 ^c	._b	._b	._b
Periventricular flaring/Intraventricular haemorrhage ^c	1.50 [0.18, 12.78]	0.56 [0.05, 6.77]	._b
Infection/sepsis ^c	0.60 [0.05, 7.41]	._b	._b
Meconium staining of amniotic fluid	0.90 [0.35, 2.29]	0.77 [0.29, 2.03]	5.45 [1.16, 25.74]
Hyperbilirubinaemia requiring phototherapy	1.39 [0.44, 4.45]	0.18 [0.02, 1.42]	._b
Socio-economic characteristics			
Advanced maternal age	2.62 [1.29, 5.32]	0.75 [0.32, 1.73]	0.81 [0.09, 6.90]
Advanced paternal age	1.50 [0.63, 3.53]	0.88 [0.36, 2.17]	._b
Maternal educational level: low to middle ^d	1.12 [0.60, 2.07]	2.88 [1.45, 5.72]	0.33 [0.06, 1.72]
Paternal educational level: low to middle ^d	0.91 [0.48, 1.72]	1.48 [0.79, 2.81]	0.28 [0.05, 1.49]
Maternal ethnicity: non-native Dutch	3.35 [1.51, 7.43]	0.86 [0.33, 2.28]	3.36 [0.62, 18.30]
Paternal ethnicity: non-native Dutch	1.46 [0.55, 3.85]	1.28 [0.47, 3.53]	8.69 [1.80, 42.06]
Multivariable logistic regression			
Advanced maternal age	2.29 [1.11, 4.76]		
Maternal ethnicity: non-native Dutch	2.93 [1.29, 6.64]		
Meconium staining of amniotic fluid			4.30 [0.85, 21.69]
Paternal ethnicity: non-native Dutch			7.16 [1.41, 36.32]

Data are presented as odds ratio (OR) and 95% confidence interval in brackets. ORs for the associations with sporadic fidgety were adjusted for age. Bold type indicates a significant association ($p < 0.05$). MA = mildly abnormal, FM = fidgety movement.

^a OR was estimated with reference to the infants who showed normal FMs in both temporal organization and quality ($n = 216$).

^b OR cannot be estimated because the characteristic did not occur in infants with mildly impaired GMs.

^c OR was estimated in the subgroup of preterm infants.

^d Low to middle educational level: below vocational college and university.

3.3. Concurrent associations between GMs and SINDA

MA GM-complexity was associated with impaired performance on SINDA's neurological and developmental scales. Infants with MA GM-complexity had a lower neurological score (Mann-Whitney U test: $p < 0.001$) and a higher risk of atypical neurological (OR = 7.62 [3.51, 16.54]) and developmental scores (OR = 2.38 [1.16, 4.88]) than infants with normal GM-complexity (Table 3). GM-complexity was not associated with atypical behavioural ratings on the socio-emotional scale.

Tests in the entire study sample and the subgroup of infants aged 9–15 weeks both indicated that the presence of mildly impaired FMs, either sporadic or exaggerated, was not associated with any of SINDA's parameters.

4. Discussion

Our study demonstrated that during GMs within the typical spectrum, the degree of GM-complexity and the characteristics of FMs are interrelated. Infants with MA GM-complexity were more likely to have mild impairments in FMs, i.e. sporadic or exaggerated FMs. MA GM-complexity, sporadic and exaggerated FMs were in particular associated with the infant's social background. However, MA GM-complexity, but not sporadic or exaggerated FMs, was associated with atypical scores on SINDA's neurological and developmental scales.

This study indicated that in the general Dutch population non-native Dutch parents, advanced maternal age and a lower maternal education level were associated with GMs with mild impairments. Non-native Dutch women experience culture and language barriers in their

access to the Dutch obstetric system. This results for instance in a delayed start of antenatal care [29,30]. The barriers are reflected in an increased perinatal mortality of infants born in non-native Dutch families compared to native Dutch families [31]. The association between higher maternal education and a lower prevalence of GMs with mild impairments may – at least in part – be attributed to the more healthy behaviour during pregnancy of mothers with a higher education, as these maternal characteristics are associated with better perinatal outcomes [32,33]. Our results underline the importance of adequate antenatal care for optimizing the infant's brain function.

In the methods section we mentioned that GMs with mild impairments at fidgety GM-age have limited predictive value [2,9,28]. This is certainly true at the level of the individual infant. However, studies also indicated that on group level infants born after a suboptimal pregnancy are prone to minor deviancies in neurological function in early infancy, i.e., GMs with mild impairments. These mild impairments, in turn, have been associated with less favourable neurodevelopmental outcomes, especially with impaired fine manipulative ability [7,27,28] and attention and externalizing behavioural problems [15] at school age. This may imply that improvement of antenatal health care, including a barrier-free access, may not only optimize the young infants' neurodevelopmental condition, but may also result in an optimization of average brain function in later childhood.

Medical prenatal and perinatal characteristics had a limited impact on GMs with mild impairments. It has been well documented that preterm birth increases the risk of MA GM-complexity and abnormal FMs [1,2]. We could not replicate this finding in the general population, presumably due to the typical low prevalence of very preterm infants in this population (< 32 weeks, $n = 6$). The small number of preterm

Table 3

Associations between general movements (GMs) and the Standardized Infant NeuroDevelopmental Assessment (SINDA).

	GM-complexity		Fidgety movements		
	Normal (n = 231)	MA (n = 52)	Clearly present (n = 216)	Mildly impaired (n = 67)	
				Sporadic (n = 60)	Exaggerated (n = 7)
Neurologic scale					
Total scores, median (range)	25 (18–28)	23 (19–28)	25 (18–28)	25 (19–28)	25 (20–27)
Atypical score (≤ 21), n (%)	15 (6)	18 (35)	23 (11)	8 (13)	2 (29)
Developmental scale					
Total scores, median (range)	10 (2–15)	10 (2–15)	10 (2–15)	11 (5–14)	11 (7–15)
Atypical score (≤ 7), n (%)	31 (13)	14 (27)	34 (16)	10 (17)	1 (14)
Socio-emotional scale					
Atypical interaction	20 (9)	5 (10)	20 (9)	5 (8)	0 (0)
Atypical emotionality	29 (13)	10 (19)	28 (13)	11 (18)	0 (0)
Atypical self-regulation	21 (9)	5 (10)	20 (9)	6 (10)	0 (0)
Atypical reactivity	8 (3)	1 (2)	9 (4)	0 (0)	0 (0)

Bold type indicates a significant difference ($p < 0.05$) in comparison with infants with normal GM-complexity or normal fidgety movements in both temporal organization and quality. MA = mildly abnormal.

infants further restricted our power to detect a significant association between neonatal morbidity and mildly impaired GMs. Nevertheless, the literature also suggested that a low 5-min Apgar score, mild abnormality on cranial ultrasound and sepsis in very preterm infants did not predict abnormal GM-complexity and FMs [34]. Previously, it had been reported that in healthy term infants hyperbilirubinaemia (with or without the requirement of phototherapy) was associated with MA GM-complexity and that the degree of hyperbilirubinaemia showed a dose-response relationship with minor neurological dysfunction [35]. Since then, the guidelines for the initiation of treatment for hyperbilirubinaemia were changed, including a lower threshold to start treatment ([36]; Dutch adaptation [37]). Our finding that moderate hyperbilirubinaemia requiring phototherapy was not associated with MA GM-complexity suggests that current early treatment strategies are effective in this respect. Meconium-stained amniotic fluid was the only neonatal factor associated with GMs with mild impairments (exaggerated FMs). The presence of meconium-stained amniotic fluid may be a sign of pathologic fetal distress, but it also has been described as a physiological event of maturation [38]. Its predictive value for developmental outcome is unclear [39]. The association between meconium-stained amniotic fluid and exaggerated FMs disappeared when parental ethnicity was taken into account. This may imply that infants with a non-native Dutch background more often have meconium in the amniotic fluid. Others reported that infants with an African and Asian background more often show meconium staining of the amniotic fluid than Caucasian infants [40,41]. Again, this suggests that infants with a non-native Dutch background may be at disadvantage in the Dutch antenatal health care system.

MA GM-complexity was associated with atypical neurological and developmental SINDA scores, but sporadic and exaggerated FMs were not. The strong association between GM-complexity and the neurological scores is perhaps not surprising because a quarter of the items of SINDA's neurological scale assess the quality of spontaneous movements. Yet, MA GM-complexity was also associated with an atypical developmental score. This finding is in line with previous reports that GM-complexity was associated with cognitive [6,7,11,15,18], language [42], and motor outcomes [5,6,19]. Mildly impaired FMs were not associated with the SINDA neurological and developmental scores. This suggests that MA GM-complexity is a more sensitive parameter of non-optimal brain function than sporadic or exaggerated FMs.

The strength of this study was the inclusion of infants representative of the Dutch population in terms of prevalence of maternal overweight or obesity, assisted reproduction, instrumental delivery, males, twins, preterm birth, small for gestational age, parental age and parental educational level and ethnicity [23]. The representativeness of parental demographic factors in particular allows the investigation of the

association between low socio-economic status and mildly impaired GMs. The relatively wide range of assessment age, from 2 to 4 months, may be regarded as the major limitation of the study, as it is well-known that sporadic FMs are age-related. We therefore adjusted for infant age in the statistical analyses and performed the analyses in the subgroup of infants aged 9 to 15 weeks, and found that the findings of both approaches did not differ. The use of SINDA to measure the neurological condition in this relatively low-risk study group may be regarded as a limitation as the validity of this instrument has only been documented in at-risk populations and its predictive validity has only been reported in two studies that followed the children to at least two years of age [24,25]. The follow-up of our participants at the age of 4–5 year is currently planned.

In conclusion, the present study - that focused on GMs in the typical spectrum - endorses the notion that GM-complexity and FMs are two different but interrelated aspects of GMs. Around half of the infants with MA GM-complexity showed sporadic or exaggerated FMs. Moreover, a MA GM-complexity and FMs with mild impairments were associated with parameters of less optimal socio-economic background. Yet, the findings suggested that MA GM-complexity is more sensitive to pick up impairments in neurological and developmental condition than FMs with mild impairments.

Declaration of competing interest

None.

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