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Predictive value of general movements' quality in low-risk infants for minor neurological dysfunction and behavioural problems at preschool age

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ABSTRACT

Background: General movement (GM) assessment is a well-established tool to predict cerebral palsy in high-risk infants. Little is known on the predictive value of GM assessment in low-risk populations.
Aims: To assess the predictive value of GM quality in early infancy for the development of the clinically relevant form of minor neurological dysfunction (complex MND) and behavioral problems at preschool age.
Study design: Prospective cohort study.
Subjects: A total of 216 members of the prospective Groningen Assisted Reproductive Techniques (ART) cohort study were included in this study. ART did not affect neurodevelopmental outcome of these relatively low-risk infants born to subfertile parents.
Outcome measures: GM quality was determined at 2 weeks and 3 months. At 18 months and 4 years, the Hempel neurological examination was used to assess MND. At 4 years, parents completed the Child Behavior Checklist; this resulted in the total problem score (TPS), internalizing problem score (IPS), and externalizing problem score (EPS). Predictive values of definitely (DA) and mildly (MA) abnormal GMs were calculated.
Results: DA GMs at 2 weeks were associated with complex MND at 18 months and atypical TPS and IPS at 4 years (all $p < 0.05$). Sensitivity and positive predictive value of DA GMs at 2 weeks were rather low (13%–60%); specificity and negative predictive value were excellent (92%–99%). DA GMs at 3 months occurred too infrequently to calculate prediction. MA GMs were not associated with outcome.
Conclusions: GM quality as a single predictor for complex MND and behavioral problems at preschool age has limited clinical value in children at low risk for developmental disorders.

1. Introduction

The assessment of the quality of general movements (GMs) is one of the best methods to predict developmental outcome in high-risk infants [1,2]. GMs are spontaneous movements involving all body parts [3]. They are present during fetal life and early infancy and they disappear around 4 months postterm, when goal-directed motor behavior emerges. Concurrent with the developmental changes in the brain, the form of GMs changes. Around term age, GMs have a 'writhing' character and in the last phase – present at 2 to 4 months postterm – GMs have a 'fidgety' character. Multiple studies in high-risk infants have demonstrated that in particular the presence of definitely abnormal (DA) GMs at 'fidgety age' is associated with a high risk for cerebral palsy (CP) [4–8]. DA GMs are characterized especially by a lack of movement complexity and variation. DA GMs in high-risk infants are also associated with minor neurological dysfunction (MND), especially with the clinically relevant form complex MND, and with behavioral problems in later life [9–11].

In contrast to the well-documented predictive validity of GM assessment in high-risk infants, little is known on the predictive value of GM quality in infants with a low risk for developmental disorders. The information available is limited to the study of Bouwstra et al. [12]. In 450 3-month-old infants, Bouwstra et al. studied the ability of DA GMs to predict serious neurodevelopmental disorders and behavioral problems in preschoolers from the general population. The results showed an association between DA GMs and major neurodevelopmental disorders, but the association was less strong than that in the high-risk populations. DA GMs were not associated with behavioral problems.

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The present study aims to assess the predictive value of definitely and mildly abnormal GMs at 2 weeks and 3 months for the development of complex MND and behavioral problems at preschool age, i.e., at 18 months and 4 years, in a group of low-risk infants. When positive or negative predictive values are good, early detection and exclusion of MND and behavioral problems may provide options for early intervention or reassurance, respectively.

To this end, we used the data collected in the Groningen Assisted Reproductive Techniques (ART) cohort study. This study aims to assess the effect of in vitro fertilization (IVF) on the child's development by comparing outcome of children born after IVF with those having been conceived naturally. The data revealed that IVF did not affect neurological and behavioral outcome up until the age of 4 years [13–18].

On the basis of the study of Bouwstra et al. [12], we hypothesize that the predictive value of DA GMs at 3 months for complex MND and behavioral problems in our group of low-risk infants is lower than that in high-risk infants. We expect that also mildly abnormal (MA) GMs are associated with complex MND and behavioral problems at preschool age, but less strongly than DA GMs. In addition, we expect that prediction of DA GMs at 2 weeks is better than that of DA GMs at 3 months, as neonatal neurological dysfunction in relatively low-risk infants often is followed by neurological normalization in infancy, to be followed by complex MND in later years [19]. Finally, we hypothesize that persistently abnormal GMs, i.e., the presence of abnormal GMs at 2 weeks and at 3 months, have the best predictive value for neurobehavioral problems, as a persistently abnormal quality of GMs during the first months after term age in high risk is associated with the highest risk for CP [8].

2. Materials and methods

2.1. Participants

The 216 participants (110 males, 106 females) were the members of the prospective Groningen ART cohort study, a prospective, assessor-blinded, follow-up study that monitors child development after ART. They were recruited between March 2005 and December 2006 at the Department of Reproductive Medicine of the University Medical Center Groningen (UMCG). The children were born following IVF with or without ovarian hyperstimulation or to subfertile couples who conceived naturally while waiting for fertility evaluation or treatment. Information on the prenatal, perinatal, and neonatal periods, parental characteristics, and socioeconomic conditions were collected from medical records and on standardized charts at the first follow-up assessment 2 weeks postterm. Table 1 provides an overview of the perinatal and social characteristics of the study group. The ethics committee of the UMCG approved the study design, and all parents provided written, informed consent for participation of their children in the study.

GM quality was assessed at 2 weeks and 3 months, neurological follow-up at 18 months and 4 years. Included in the current study were the infants with at least one appropriate recording of GMs and one follow-up assessment at preschool age. At 2 weeks, data of 6 infants were missing: 2 had missed their appointment and another 4 had been crying. At 3 months, data of 4 infants were missing, 7 children did not show up at 18 months, and at 4 years, 21 children were lost to follow-up. Attrition was mainly due to logistical problems or assessment burden. One girl died at 3 weeks of age from the consequences of a congenital heart disorder. Background characteristics of the infants included in the study did not differ from those of the children who were excluded from the analyses (data not shown).

2.2. GM assessment

GM quality was assessed at 2 weeks and 3 months postterm by two assessors (K.M. and M.H.-A; for details see Middelburg et al. [14]). Spontaneous movements in supine position were videotaped for 5–10 min. The aim was to record the infant's motility in an awake, active, and not-crying behavioral state. Quality of GMs was classified into four different categories: two normal types and two abnormal types [9]. The two subtypes of normal GMs are normal–optimal GMs, which are characterized by abundant variation, complexity, and fluency, and normal–suboptimal movements, which have a sufficient degree of variation and complexity, but lack fluency. Abnormal GMs also lack fluency; they are subdivided into MA GMs, which are characterized by insufficient variation and complexity and DA GMs, which are virtually devoid of variation and complexity. The reliability of the GM assessment is good, including for this study [9,13].

Table 1
Participant characteristics.

Characteristics	Study group, $n = 216$
Male/female	110/106
Birth characteristics	
Gestational age (weeks), median (range)	39.9 (30–43)
Preterm birth <37 weeks, *n* (%)	20 (9)
Birth weight (g), mean (SD)	3453 (568)
Low birth weight <2500 g, *n* (%)	12 (6)
Small for gestational age,* *n* (%)	5 (2)
Signs of fetal distress,** *n* (%)	77 (36)
Caesarean section, *n* (%)	49 (23)
Neonatal characteristics	
Apgar score 5 min <7,[a] *n* (%)	1 (1)
Neonatal intensive care admission, *n* (%)	10 (5)
Parental characteristics	
Maternal age at conception in years, median (range)	32.9 (22–41)
Paternal age at conception in years,[b] median (range)	35.1 (26–56)
High education level mother,*** *n* (%)	85 (39)
High education level father,[c,***] *n* (%)	81 (38)

* Birth weight for gestational age is below 2 standard deviations compared with the Dutch reference population (Dutch reference tables, perinatal Registration Netherlands).
** Signs of fetal distress denoted by meconium stained amniotic fluid and/or cardiotocographic signs and/or acidosis.
*** University education or vocational colleges.
[a] Missing data $n = 6$.
[b] Missing data $n = 5$.
[c] Missing data $n = 4$.

2.3. Assessment of neurological condition at 18 months and 4 years

At 18 months and 4 years, the standardized and age-specific neurological examination according to Hempel (1993) was used to assess MND [20]. The Hempel examination has been developed to evaluate MND at preschool age. It assesses MND in five domains of functions: fine motor function, gross motor function, posture and muscle tone, reflexes, and visuomotor function [21]. Each of the domains can be scored as typical or deviant. Findings are classified as major neurological dysfunction, complex MND, simple MND, or neurologically normal. Major neurological dysfunction implies the presence of a distinct neurological syndrome, such as CP. Complex MND implies the presence of two or more deviant domains; simple MND implies the presence of one deviant domain. Neurologically normal implies the absence of deviant domains or the presence of only deviant reflexes [21]. Simple MND has limited clinical significance and reflects the presence of a normal, but non-optimally wired brain. On the other hand, complex MND represents the clinically relevant form of MND and is associated with behavioral and learning disorders [19]. The reliability of the Hempel examination is satisfactory (κ scores for various items: 0.62–1.00). Information on the predictive validity is lacking thus far [21]. The assessments were carried out by trained assessors supervised by M.H.-A. All assessors and the supervisor were blind to prenatal and perinatal history, and to GM quality.

2.4. Assessment of child behavior at 4 years

Child behavior at 4 years was evaluated with the Dutch version of the Child Behavior Checklist (CBCL) for children aged 1½ year to