Motor behaviour in infancy is associated with neurological, cognitive, and behavioural function of children born to parents with reduced fertility

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AIM To evaluate the associations between motor development in infancy and developmental outcomes at school age.

METHOD Participants were 195 children (99 males, 96 females; mean age [SD] 9y 3mo [3mo], range 8y 4mo–10y 11mo) born to couples whose reduced fertility was or was not treated with assisted reproductive technologies. Motor behaviour was assessed at 4, 10, and 18 months with the Infant Motor Profile (IMP). IQ, neurological optimality score (NOS), and behavioural problem scores were measured at 9 years with the Wechsler Abbreviated Scale of Intelligence, minor neurological dysfunction assessment, and the Child Behavior Checklist respectively.

RESULTS Children with a slow developmental trajectory in the IMP-domain adaptability had an IQ 12.6 points lower (95% confidence interval [CI] 4.7–20.4) and an NOS 3.4 points lower (95% CI 0.7–6.2) at 9 years of age than children with typical adaptability development. Children with a slow developmental trajectory in the IMP-domain performance had an IQ 5.0 points lower (95% CI 0.7–9.3) than children with typical performance development. A non-optimal trajectory in IMP-variation and a fluctuating trajectory in IMP-fluency were associated with higher internalizing scores of 3.6 and 5.8 points respectively, than infants with optimal IMP-domain trajectories.

INTERPRETATION In relatively low-risk children, motor behaviour in infancy was associated with neurological, cognitive, and behavioural function at school age.

Motor behaviour is a developmental domain that changes remarkably in infancy. The early emergence of motor behaviour suggests its pivotal role in further development. Indeed, we have come to understand that neural activity is organized by means of continuous inter-regional interaction in wide-spread neural networks, causing a strong inter-relation of motor and cognitive development from an early age.1,2

The assessment of motor development has always been one of the cornerstones of the evaluation of infant development. Infant motor behaviour may be evaluated in terms of milestones and by assessment of movement quality. Assessing milestones assists in the early detection of infants at risk of developmental disorders. In addition, it is known that in typically developing children attainment of milestones is weakly, but significantly, associated with cognitive and motor outcomes and adaptive behaviours at school age.1,4

Gradually it has become clear that the quality of motor behaviour in infancy is an important tool in predicting developmental outcomes, including cerebral palsy.5 Tools to assess quality of motor behaviour include the General Movement Assessment6 and the Test of Infant Motor Performance7 in young infants, and the Infant Motor Profile (IMP) in infants aged at least 3 months.8 The IMP assesses motor behaviour in four qualitative domains (variation, adaptability, symmetry, and fluency) and one quantitative milestone domain ‘performance’. Two domains are novel and based on the Neuronal Group Selection theory: variation and adaptability.2 Variation refers to the size of the motor repertoire. Adaptability is the ability to select efficient strategies according to the situation and develops between 6 and 18 months at function-specific ages. Adaptive behaviour emerges through implicit motor learning from active trial-and-error experiences.2

Previously we have reported that reduced variation, reduced adaptability, and a slower increase in performance scores were associated with IQ scores at 4 years of age.9 That study was based on the longitudinal data of the Groningen Assistive Reproductive Technologies (ART) cohort. This cohort was designed to study the associations...
between components of in vitro fertilization and developmental outcome. In the longitudinal ART cohort we not only collected data on motor development during infancy by means of the IMP at 4, 10, and 18 months, but also on developmental outcome at 4 years and, recently, at 9 years. The ART cohort studies revealed that the in vitro fertilization-components were not associated with IMP-scores during infancy,\(^\text{9,11,12}\) nor with outcomes at 4 and 9 years.\(^\text{10}\)

Considerable changes in brain organization occur between 4 and 9 years of age.\(^\text{13}\) Therefore, the aim of the current study was to assess the prediction of early motor development on developmental outcome at school age, by evaluating associations between motor behaviour across infancy and long-term outcomes in several developmental domains at 9 years. Knowing that motor development is a dynamic process driven by continuous interaction between the nervous system and the environment,\(^\text{2}\) we used development trajectories based on longitudinal data rather than motor scores at a single age in order to understand the potential predictions of the progression in motor skills acquisition and the developmental changes in movement quality. We hypothesized that unfavourable trajectories with lower scores on the IMP-domains variation, adaptability, and performance are associated with a lower IQ, a less optimal neurological condition, and more behavioural problems at age 9 years in the ART cohort, who were at a relatively low risk of neurodevelopmental disorder.\(^\text{14}\)

**METHOD**

**Participants**

The study group consisted of 249 children who participated in the Groningen ART cohort study. They were recruited at the Department of Reproductive Medicine of the University Medical Center Groningen between March 2005 and December 2006. Detailed information on recruitment has been provided elsewhere.\(^\text{15}\) In brief, the participants were born after in vitro fertilization or intracytoplasmic sperm injection, with or without ovarian stimulation, or conceived naturally to couples with reduced fertility. We previously demonstrated that the in vitro fertilization-procedures did not affect developmental outcome at 9 years.\(^\text{11,12}\) Therefore, we pooled the ART-subgroups to form one study group. The group included singletons and twins (Table 1 and Table S1, online supporting information). Prenatal, perinatal, and socio-economic information was collected on standardized charts at 2 weeks of age.\(^\text{15}\) Socio-economic information was updated at the follow-up visit at 9 years.

The study design was approved by the Medical Ethics Committee of the University Medical Center Groningen (METc 2005/003) and written, informed consent was obtained from the parents.

**Assessment of motor behaviour in infancy**

Infant motor behaviour was assessed longitudinally at 4, 10, and 18 months using the IMP, a video-based assessment tool used to qualitatively evaluate motor behaviour in infants aged 3 to 18 months.\(^\text{8}\) During the assessment, self-produced movements are observed in supine, prone, sitting, standing, and walking and during reaching, grasping, and manipulation. The IMP comprises 80 items in five domains: variation, adaptability, symmetry, fluency, and performance. The domain scores are individually obtained by calculating the percentage of the raw score relative to the maximal score. Adaptability scores are calculated only in infants aged 6 months and older. The total IMP score is calculated as the mean of the five (or four, in infants <6mo) domain scores.

The infants of the ART cohort had their IMP assessments more than 10 years ago, when the IMP was relatively new. Since then, the assessment method has been fine-tuned. This resulted in, among other things, the addition of specific rules on when the section on the supine

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**What this paper adds**

- Motor behaviour in infancy is associated with developmental outcomes at school age.
- Infant motor adaptability and motor milestone performance are associated with 9-year IQ.
- Infant motor adaptability is also associated with neurological condition at school age.
- Infant motor adaptability has a stronger association with IQ at 9 years than at 4 years.
- Movement variation and fluency in infancy are associated with long-term behavioural outcome.

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**Table 1: Background characteristics of the study group**

| Characteristics                              | Study group (n=195) |
|----------------------------------------------|--------------------|
| **Prenatal and perinatal characteristics**   |                    |
| Male, n (%)                                  | 99 (50.8)          |
| Twins, n (%)                                 | 24 (12.3)          |
| Gestational age (wks), mean (SD)             | 39.2 (2.2)         |
| Preterm birth (<37wks), n (%)                | 32 (15.7)          |
| Birthweight (g), mean (SD)                   | 3327.6 (665.5)     |
| Small for gestational age, n (%)\(^a\)       | 6 (3.1)            |
| **Parental characteristics**                 |                    |
| Time to pregnancy (y:mo), median (25th–75th centile) | 3:2 (1:10–5:0)   |
| Maternal age at conception (y:mo), mean (SD) | 32:11 (3:5)        |
| Maternal educational level (vocational college or higher), n (%) | 83 (42.6) |
| **Neurodevelopmental outcomes at 9 years**   |                    |
| Available for Wechsler Abbreviated Scale of Intelligence, n | 187                |
| Full-scale IQ, mean (SD)                     | 114.1 (14.2)       |
| Verbal IQ, mean (SD)                         | 114.0 (15.6)       |
| Performance IQ, mean (SD)                    | 111.2 (14.4)       |
| Available for Groningen Assessment of MND, n | 191                |
| Typical neurological function, n (%)         | 30 (15.7)          |
| Simple MMD, n (%)                            | 94 (49.2)          |
| Complex MND, n (%)                           | 67 (35.1)          |
| NOS, mean (SD)                               | 52.2 (4.8)         |
| Available for Child Behavior Checklist for Ages 6–18, n | 190                |
| Total behavioural problem, mean (SD)         | 48.3 (10.1)        |
| Internalizing problem, mean (SD)             | 49.6 (9.8)         |
| Externalizing problem, mean (SD)             | 46.9 (9.9)         |

\(^a\)Defined as birthweight for gestational age less than 2 SD compared with Dutch reference population. MND, minor neurological dysfunction; NOS, neurological optimality score.
items could be classified as ‘not assessed’. We applied the new rules of the IMP’s final version to the IMP assessments of the ART cohort, implying that the IMP data presented in the current paper differ slightly from those reported by Heineman et al.9 Nevertheless, we replicated Heineman’s analyses with the current IMP scores and the results remained basically the same (Figure S1 and Tables S2 and S3, online supporting information). This consistency also demonstrates that the construct of the IMP did not change by the application of the new rules.

**Follow-up assessments at 9 years**

Neurological, cognitive, and behavioural outcomes were evaluated respectively with the Wechsler Abbreviated Scale of Intelligence,16 the Groningen assessment of minor neurological dysfunction (MND),17 and the Dutch version of Child Behavior Checklist for Ages 6–18.18 The assessors (DK, MDO) were unaware of the child’s prenatal and perinatal history or IMP results.

The Wechsler Abbreviated Scale of Intelligence is a standardized instrument to evaluate cognitive function in individuals aged 6 to 89 years.16 It is the short form of the full Wechsler scales and consists of four subtests: vocabulary, similarities, block design, and matrix reasoning. The first two comprise the verbal scale and yield the verbal IQ; the latter two comprise the performance scale and yield the performance IQ. Full-scale IQ can be calculated on the basis of the four subtests. Verbal IQ, performance IQ, and full-scale IQ are standardized and normed with a mean (SD) of 100 (15).

The Groningen assessment of MND is a criterion-referenced assessment tool to evaluate the neurological integrity of the brain in children at least 4 years of age.17 It has 64 items that evaluate motor and sensorimotor functions. The results are summarized into eight domains of dysfunction: dysfunctional posture and muscle tone regulation, dysfunctional reflexes, mild dyskinesia, mild problems in coordination, mild problems in fine manipulative ability, excessive associate movements, mild cranial nerve dysfunction, and mild sensory dysfunction. On the basis of the examination, children are classified as neurologically typical, simple MND, complex MND, or atypical. The latter means the presence of a clear neurological syndrome, such as cerebral palsy. At school age simple MND denotes the presence of one or two dysfunctional domains and complex MND, the clinically relevant form, indicates the presence of at least three dysfunctional domains.17 The assessment may also be summarized by means of the neurological optimality score (NOS; range 0–64), which is calculated by summing the number of items scored within the optimal range. This turns the NOS into a sensitive instrument to evaluate subtle differences in neurological condition.

The Child Behavior Checklist for Ages 6–18 is a parent-report questionnaire.18 It comprises 113 items in eight behavioural syndrome domains (anxious/depressed, withdrawn/depressed, somatic complaints, social problems, thought problems, attention problems, rule-breaking behaviour, and aggressive behaviour) and other problems. Scores on the first three domains result in the internalizing problem score; scores in the last two domains result in the externalizing problem score. We used the normalized T-scores of the internalizing, externalizing, and total problem scores, with the 50th centile being 50. Higher scores indicate more problematic behaviour.

**Statistical analyses**

The baseline characteristics of the children included in the 9-year follow-up and the children not assessed at 9 years were compared by independent *t*-test and Pearson’s *χ²* test for numerical and categorical variables respectively. Next, latent class growth modelling was used to distinguish developmental trajectories in IMP domain scores and the total IMP score using the data at 4, 10, and 18 months. Latent class growth modelling identifies clusters of individuals after a similar developmental trajectory on an observed variable by fitting a group-based model.19 Quadratic polynomials were assigned in modelling the trajectories as a quadratic function of age described the longitudinal IMP scores best.9,20 Note that linear polynomials were used specifically for IMP-domain adaptability as adaptability scores were only available at two ages (10mo and 18mo). One, two, and three clusters were sequentially fitted into the latent growth model to test the number of trajectory groups, and the best model was chosen based on the Bayesian information criterion. According to the results, each child was categorized into one of the trajectory groups. The average posterior probability (AvePP) of each trajectory group was calculated to indicate the certainty of group assignment, where a minimum value of at least 0.7 should be achieved.19 Finally, multivariable linear regression, or logistic regression with adjustment of confounding variables, was applied to examine the contribution of developmental motor trajectories to 9-year outcomes. In our previous studies, time to pregnancy (the time it took couples to achieve pregnancy after the start of regular unprotected intercourse), small for gestational age (birthweight below the 10th centile), and maternal education have been recognized as confounding variables.21,22 In addition, we adjusted the analyses of all outcomes for preterm birth and sex. All analyses were conducted with SAS software (SAS Institute, Cary, NC, USA) and latent class growth modelling was processed using the TRAJ procedure. The level of statistical significance for the tests was set at 0.05.

**RESULTS**

**Participants**

Of the 249 original enrolees of the study, 195 (78.3%) were developmentally assessed at 9 years (99 males, 96 females; mean age [SD] 9y 3mo [3mo], range 8y 4mo–10y 11mo). Their background characteristics are shown in Table 1 and Table S1. The children with follow-up differed significantly from the children without follow-up only in terms of maternal age at conception mean age (SD) 32 years 11 months (3y 5mo) in children with follow-up,
31 years 9 months (3y 7mo) in children without follow-up ($p=0.033$).

**Developmental trajectories of IMP scores**

Missing data precluded trajectory calculations in two children. The results of latent class growth modelling of scores in IMP-domain variation suggested the presence of two groups: a larger ‘non-optimal group’ ($n=164$, AvePP=0.97) and a smaller ‘optimal group’ ($n=83$, AvePP=0.79) (Fig. 1a). Modelling of the scores in the IMP adaptability domain revealed three groups: a ‘typical group’ (containing the majority of the children and representing the trajectory of typical development, $n=222$, AvePP=0.90), a ‘rapid group’ ($n=8$, AvePP=0.98), and a ‘slow group’ ($n=17$, AvePP=0.74) (Fig. 1b). In the development of symmetry, one group was determined as only four children showed deviant symmetry scores from the age of 10 months onward (Fig. 1c). Analyses for associations with 9-year outcomes were, therefore, not conducted. In the fluency domain, three groups were distinguished: a large ‘fluctuating group’ ($n=154$, AvePP=0.98), a ‘high group’ ($n=32$, AvePP=0.95), and a ‘low group’ ($n=61$, AvePP=1.00) (Fig. 1d). In the performance domain, two groups were present: a ‘typical group’ ($n=166$, AvePP=0.94) and a ‘slow group’ ($n=81$, AvePP=0.87) (Fig. 1e). Finally, the results of latent class growth modelling of the total IMP scores indicated two groups: a ‘typical group’ ($n=209$, AvePP=0.94) and a ‘slow group’ ($n=38$, AvePP=0.82) (Fig. 1f).

**IMP developmental trajectories and cognitive outcome**

The IMP-domains adaptability and performance were related to IQ. Specifically, adaptability was associated with both verbal IQ and performance IQ, and IMP performance was associated with performance IQ (Table 2 and Table S4, online supporting information). Children in the slow adaptability group had a full-scale IQ 12.6 points lower (95% CI –20.4 to –4.7), a verbal IQ 11.4 points lower (95% CI –20.1 to –2.7), and a performance IQ 11.5 points lower (95% CI –20.1 to –2.9) than the children in the typical group. Children in the slow performance group had a full-scale IQ 5.0 points lower (95% CI –9.3 to –0.7) and a performance IQ 6.3 points lower (95% CI –10.9 to –1.7) than the children in the typical group. The other IMP domains were not associated with either the verbal IQ, performance IQ, or full-scale IQ.

The total IMP score was associated with verbal IQ. Children in the slow group had a verbal IQ 6.5 points lower than the children in the typical group (95% CI –12.7 to –0.2). The performance IQ and full-scale IQ in children in the slow group and typical group did not differ.

**IMP developmental trajectories and neurological outcome**

None of the IMP domains nor the total IMP scores were associated with the presence of complex MND. The IMP domain adaptability was associated with the NOS (Table 3 and Table S5, online supporting information). Children in the slow adaptability group had an NOS 3.4 points lower than children in the typical group (95% CI –6.2 to –0.7). There was no difference between children in the rapid adaptability group and typical group. The other IMP domains and the total IMP score were not associated with the NOS.

**IMP developmental trajectories and behavioural outcome**

The IMP domains variation and fluency were associated with internalizing problems. Children in the non-optimal variation group (50.6 [SD 9.7]) had a higher internalizing score than children in the optimal group (47.5 [SD 9.8]) (adjusted difference 3.6, 95% CI 0.6–6.7, $p=0.020$). Also, children in the fluctuating fluency group (50.9 [SD 9.5]) had a higher internalizing score than children in the high fluency group (44.8 [SD 9.8]) (adjusted difference 5.8, 95% CI 1.2–10.4, $p=0.014$). However, children in the low fluency group (48.4 [SD 10.8]) showed a comparable internalizing score with children in either the fluctuating group or the high fluency group.

None of the IMP domains nor total IMP scores were associated with the total behavioural problem and externalizing problem scores.

**DISCUSSION**

In line with our hypotheses, motor behaviour assessed by the IMP in infancy was associated with neurological, cognitive, and behavioural function at 9 years. The IMP adaptability domain was related to IQ and neurological function, the performance domain was also associated with IQ, and the domains variation and fluency were associated with internalizing behavioural problems. Early motor behaviour was clearly associated with IQ. The IMP performance domain was associated with performance IQ. This finding is in line with other studies that reported advanced performance in motor milestones predicted higher cognitive function, particularly executive function, but not verbal ability, at school age.23 Perhaps the association may be attributed to the shared neurological origin in the fronto-striatal circuits in the development of motor performance and executive function.24 Moreover, the strongest association was found between the adaptability domain and IQ. Results from imaging studies revealed a shift from a diffuse to focal and task-specific activity pattern when a motor behaviour becomes adapted,25 and when a cognitive ability is mastered.26 The shift implies more efficient processing as the magnitude of activation in relevant areas increases, with an attenuation of activation in areas not critically involved in the task. Pruning of irrelevant connections especially occurs from middle childhood (around 8y) and early adulthood.26,27 This may further explain why we only found weak associations between adaptability during infancy and IQ at 4 years,9 but substantially stronger associations between adaptability and IQ at 9 years.

Interestingly, adaptability predicted not only performance IQ but also verbal IQ. Recent studies demonstrated
Figure 1: Latent class growth modelling of the Infant Motor Profile (IMP) scores: developmental trajectories of domains (a) variation, (b) adaptability, (c) symmetry, (d) fluency, (e) performance, and (f) total IMP score. Adaptability scores at 4 months were not applicable. The solid lines indicate the group that contained the majority of the children.
the important involvement of motor circuits in learning language: the premotor and motor cortex provide movement-related information for perceiving and comprehending language. In addition, performance of a movement and listening to the verb corresponding to that movement are associated with similar task-specific activity in the inferior frontal areas.28

It is not surprising that less advanced adaptability in infancy was related to MND. The association between the IMP adaptability domain and the NOS indicates a conceptual similarity between the two descriptors of motor behaviour, with both emphasizing the use of adequate motor strategies in accomplishing motor-related tasks.17

Children with optimal variation and high fluency had better behavioural outcomes, specifically, a lower internalizing problem score. The largest discrepancy between the variation trajectories and between the fluency trajectories occurred at 4 months. Our results supported the prediction of motor behaviours with reduced variation and fluency in early infancy (i.e. the atypical general movements) to later internalizing problems.29 However, the majority of children in this study showed a non-optimal variation trajectory and a fluctuating fluency trajectory, which could be attributed to typical development10 or the influence of reduced fertility.22 As the differences in internalizing scores between the groups with optimal and non-optimal variation and fluency are small (3.6 and 5.8 points respectively), the predictive power of IMP variation and fluency scores for later behavioural problems is regarded as limited.

The strengths of this study are the longitudinal design and detailed assessments of motor behaviour. Our assessments captured differences in the trajectories of infant motor development and allowed the exploration for their associations with multidimensional developmental outcomes at 9 years. One limitation is the relatively high attrition rate after infancy of 22%; it is, however, considered acceptable for studies with a 9-year follow up.31 The major limitation is the representativeness of study sample. Thirty-five percent of our children were diagnosed with complex MND. This rate is much higher than the prevalence rate after infancy of 22%; it is, however, considered acceptable for studies with a 9-year follow up.31 The major limitation is the representativeness of study sample.

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Only the Infant Motor Profile (IMP)-domains showing a significant association with IQ and the total IMP scores were included in the table. Bold type indicates p<0.05. Differences in comparison with the typical group was tested by linear regression model with adjustment of confounding variables. The assumptions of linear regression analysis on IQs were all satisfied. Confounding variables were small for gestational age, time to pregnancy, maternal education, preterm birth, and sex.

| Groups with specific IMP-domain score trajectories | Total IMP score trajectories |
|-----------------------------------------------|-----------------------------|
| Groups with specific IMP-domain score trajectories | Only the Infant Motor Profile (IMP)-domains showing a significant association with neurological outcome and the total IMP scores were included in the table. Bold type indicates p<0.05. Differences in comparison with the typical group was tested by logistic regression model with adjustment of confounding variables. The assumptions of regression analyses were all satisfied. Confounding variables for complex MND were small for gestational age, maternal education, preterm birth, and sex; confounding variables for NOS were small for gestational age, maternal education, preterm birth, and sex. |

Table 2: Relationship between developmental motor trajectories in infancy and 9-year cognitive outcomes

| Groups with specific total IMP score trajectories | NOS |
|-----------------------------------------------|-----|
| Groups with specific total IMP score trajectories | Only the Infant Motor Profile (IMP)-domains showing a significant association with neurological outcome and the total IMP scores were included in the table. Bold type indicates p<0.05. Differences in comparison with the typical group was tested by logistic regression model with adjustment of confounding variables. The assumptions of regression analyses were all satisfied. Confounding variables for complex MND were small for gestational age, maternal education, preterm birth, and sex; confounding variables for NOS were small for gestational age, maternal education, preterm birth, and sex. |

Table 3: Relationship between developmental motor trajectories in infancy and 9-year neurological outcomes
average than the norms, presumably related to the socially advantaged status of the families with reduced fertility levels.\textsuperscript{1,4} Therefore, our results cannot be generalized to the general population.

CONCLUSION
Our study demonstrated that developmental trajectories of motor behaviour in infancy were associated with neurological, cognitive, and behavioural function at school age in relatively low-risk children (i.e. in children born to couples with reduced fertility). Reduced adaptability and a slower increase in performance scores were associated with a lower IQ. Reduced adaptability was also associated with a less optimal neurological condition; non-optimal variation and fluctuating fluency were associated with more internalizing behavioural problems.

Future research to elucidate these relationships in the general population and groups of high-risk infants is encouraged to further appreciate the clinical value of the assessment of early motor behaviour and to determine the earliest age at which infant risk profiles can predict developmental outcome.

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SUPPORTING INFORMATION
The following additional material may be found online:

Figure S1: Latent class growth modelling of IMP scores
Table S1: Background characteristics of the study group (full version)
Table S2: Correlations between IMP scores and IQ at 4 years of age
Table S3: Relations between IMP score trajectories in infancy and IQ at 4 years of age
Table S4: Relationship between developmental motor trajectories in infancy and 9-year cognitive outcomes (full version)
Table S5: Relationship between developmental motor trajectories in infancy and 9-year neurological outcomes (full version)

REFERENCES
1. Diamond A. Close interrelation of motor development and cognitive development and of the cerebellum and prefrontal cortex. Child Dev 2000; 71: 44–56.
2. Hadders-Algra M. Early human motor development: From variation to the ability to vary and adapt. Neurosci Biobehav Rev 2018; 90: 411–27.
3. Ghassabian A, Sundaram R, Bell E, Bello SC, Kus C, Yeung E. Gross motor milestones and subsequent development. Pediatrics 2016; 138: e20154372.
4. Murray GK, Jones PB, Kuh D, Richards M. Infant developmental milestones and subsequent cognitive function. Ann Neurol 2007; 62: 128–36.
5. Bosanquet M, Copeland L, Ware R, Boyd R. A systematic review of tests to predict cerebral palsy in young children. Dev Med Child Neurol 2013; 55: 418–26.
6. Perchtl HF. Qualitative changes of spontaneous movements in fetus and preterm infant are a marker of neurological dysfunction. Early Hum Dev 1990; 23: 151–8.
7. Campbell SK, Kolobe TH, Osten ET, Lenke M, Girolami GL. Construct validity of the test of infant motor performance. Phys Ther 1995; 75: 585–96.
8. Heineman KR, Bos AF, Hadders-Algra M. The Infant Motor Profile: a standardized and qualitative method to assess motor behaviour in infancy. Dev Med Child Neurol 2008; 50: 275–82.
9. Heineman KR, Schendelaar P, Van den Heuvel ER, Hadders-Algra M. Motor development in infancy is related to cognitive function at 4 years of age. Dev Med Child Neurol 2018; 60: 1149–55.
10. Schendelaar P, Heineman KR, Heineman MJ, et al. Movement variation in infants born following IVF/ICSI with and without ovarian hyperstimulation. Early Hum Dev 2013; 89: 507–13.
11. Drenth Olivares M, Kuiper DR, Haadsma ML, Heineman KR, Heineman MJ, Hadders-Algra M. IVF procedures are not, but subfecundity is associated with neurological condition of 9-year-old offspring. Early Hum Dev 2019; 129: 38–44.
12. Heineman KR, Kuiper DB, la Bastide-van Gemert S, Heineman MJ, Hadders-Algra M. Cognitive and behavioural development of children born after IVF at age 9 years. Hum Reprod 2019; 34: 2193–200.
13. Hadders-Algra M. Two distinct forms of minor neurological dysfunction: perspectives emerging from a review of data of the Groningen Perinatal Project. Dev Med Child Neurol 2002; 44: 561–71.
14. Bay B, Mortensen EL, Kesmodel US. Assisted reproduction and child neurodevelopmental outcomes: a systematic review. Fertil Steril 2011; 100: 844–53.
15. Middelburg KJ, Heineman MJ, Bos AF, Pereboom M, Fidler V, Hadders-Algra M. The Groningen ART cohort study: ovarian hyperstimulation and the in vitro procedure do not affect neurological outcome in infancy. Hum Reprod 2009; 24: 3119–26.
16. Wechsler D. Manual for the Wechsler Abbreviated Scale of Intelligence. San Antonio, TX: The Psychological Corporation, 1999.
17. Hadders-Algra M. Neurological examination of the child with minor neurological dysfunction. London: MacKeith Press, 2010.
18. Achenbach TM, Rescorla LA. Manual for the ASEBA School–Age Forms & Profiles. Burlington, VT: University of Vermont, Research Center for Children, Youth, & Families, 2001.
19. Nagin DS. Group-Based modelling of development. Cambridge: Harvard University Press, 2005.
20. Heineman KR, la Bastide-van Gemert S, Fidler V, Middelburg KJ, Bos AF, Hadders-Algra M. Construct validity of the Infant Motor Profile: relation with prenatal, perinatal, and neonatal risk factors. Dev Med Child Neurol 2010; 52: e209–15.
21. Schendelaar P, Van den Heuvel ER, Heineman MJ, et al. Increased time to pregnancy is associated with less optimal neurological condition in 4-year-old siblings, in vitro fertilization itself is not. Hum Reprod 2014; 29: 2773–86.
22. Schendelaar P, La Bastide-Van Gemert S, Heineman MJ, et al. Subfertility factors rather than assisted conception factors affect cognitive and behavioural development of 4-year-old siblings. Reprod Biomed Online 2016; 33: 752–62.
23. Piek JP, Dawson L, Smith LM, Gasson N. The role of early fine and gross motor development on later motor and cognitive ability. Hum Mov Sci 2008; 27: 668–81.
24. Hadders-Algra M. Variation and variability: key words in human motor development. Phys Ther 2010; 90: 1823–37.
25. Nishiyori R, Bisconti S, Meehan SK, Ulrich BD. Developmental changes in motor cortex activity as infants develop functional motor skills. Dev Psychobiol 2016; 58: 773–83.
26. Durston S, Davidson MC, Tottenham N, et al. A shift from diffuse to focal cortical activity with development. Dev Sci 2006; 9: 1–8.
27. Khundrakpam BS, Reid A, Brauer J, et al. Developmental changes in organization of structural brain networks. Cereb Cortex 2011; 23: 2072–85.
28. Palvermuller F, Fadiga L. Active perception: sensorimotor circuits as a cortical basis for language. Nat Rev Neurosci 2010; 11: 351–60.
29. Hadders-Algra M, Bouwstra H, Groen SE. Quality of general movements and psychiatric morbidity at 9 to 12 years. Early Hum Dev 2009; 85: 1–6.
30. Bouwstra H, Dijkstra GR, Grooten HM, et al. Prevalence of abnormal general movements in three-month-old infants. Early Hum Dev 2009; 85: 399–403.
31. Fewtrell MS, Kennedy K, Singhal A, et al. How much loss to follow-up is acceptable in long-term randomised trials and prospective studies? Arch Dis Child 2008; 93: 458–61.