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Longer duration of gestation in term singletons is associated with better infant neurodevelopment

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ABSTRACT

Background: Longer gestation at term and post-term age is associated with increased perinatal mortality. Nonetheless, recent neuroimaging studies indicated that longer gestation is also associated with better functioning of the child's brain.

Aims: to assess whether longer gestation in term and post-term (in short: term) singletons is associated with better infant neurodevelopment.

Study design: cross-sectional observational study.

Subjects: Participants were all singleton term infants ($n = 1563$) aged 2–18 months of the IMP-SINDA project that collected normative data for the Infant Motor Profile (IMP) and Standardized Infant NeuroDevelopmental Assessment (SINDA). The group was representative of the Dutch population.

Outcome measures: Total IMP score was the primary outcome. Secondary outcomes were atypical total IMP scores (scores <15th percentile) and SINDA's neurological and developmental scores.

Results: Duration of gestation had a quadratic relationship with IMP and SINDA developmental scores. IMP scores were lowest at a gestation of 38.5 weeks, SINDA developmental scores at 38.7 weeks. Next, both scores increased with increasing duration of gestation. Infants born at 41–42 weeks had significantly less often atypical IMP scores (adjusted OR [95 % CI]: 0.571 [0.341–0.957] and atypical SINDA developmental scores (adjusted OR: 0.366 [0.195–0.688]) than infants born at 39–40 weeks. Duration of gestation was not associated with SINDA's neurological score.

Conclusions: In term singleton infants representative of the Dutch population longer gestation is associated with better infant neurodevelopment scores suggesting better neural network efficiency. Longer gestation in term infants is not associated with atypical neurological scores.

1. Introduction

It is well-known that preterm birth is associated with an increased risk of perinatal mortality and neurodisability [1,2]. The risk increases with decreasing gestational age at birth [1,2]. But also in pregnancies lasting longer than 37 weeks and 0 days gestational age matters for infant outcome. Between 37 and 42 weeks the risk of perinatal mortality increases with longer duration of gestation [3,4]. The increase is especially due to the increase in antepartum stillbirth up to 3.18 per 1000

pregnancies at 42 weeks [4].

Gradually, also information is emerging on the association between the duration of gestation and neurodevelopmental outcome of live born singleton term and post-term (in short: term) infants. Early term birth, i. e., birth at 37 weeks 0 days through 38 weeks 6 days of gestation (in short: 37 to 38 weeks) [5] is associated with less favourable cognitive outcome [6] and an increased risk of psychiatric disorders. [7] The latter study is a registry based Danish study of individuals born between 1978 and 2016. It also suggested that a higher gestational age at birth beyond

Abbreviations: BMI, body mass index; CI, confidence interval; IMP, Infant Motor Profile; OR, Odds Ratio; P15, 15th percentile; SINDA, Standardized Infant NeuroDevelopmental Assessment.

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the age of 38 weeks was associated with less psychiatric morbidity [7]. The finding of a neurodevelopmental benefit of increasing duration of gestation at term age corresponds to other recent findings. First, the novel analysis of the data of the US Collaborative Perinatal Project of children born in 1959–1976 indicated that cognitive performance in term born children increased with increasing gestational age at birth up to 40 or 41 weeks of gestation [8]. The study also suggested that this effect had disappeared at school-age. Second, the study of Figlio et al. including children born in Florida in 1994–2002 reported that children delivered at 41 weeks of gestation had better cognitive scores than term children with shorter gestations [9]. Third, two neuroimaging studies indicated that longer gestation in term born children was associated with a larger brain volume [10] and a better neural network efficiency at school age [11]. It should be noted, however, that Figlio's study also showed that the cognitive benefit of a longer gestation was accompanied with a higher risk of physical disability, such as orthopaedic, speech or sensory impairments [9]. In addition, the review and meta-analysis of Glover Williams and Odd [12] indicated that the suggested beneficial effect of a longer duration of gestation at term may change into an unfavorable effect from the gestational age of 42⁺ weeks onwards.

The above implicates that two cognitive outcome studies evaluating perinatal care occurring at least two decades ago and two recent neuroimaging studies indicate that a longer duration of gestation at term age is associated with better neurocognitive outcome. Yet, Figlio's study showed that a longer gestation may also carry a higher risk of physical disability [9].

Data on the relation between gestational age at term birth and neurodevelopmental function in recently born children are lacking. The IMP-SINDA project offered an opportunity to study the association between the duration of gestation at term age and neurodevelopment in a group of singleton infants representative of the Dutch population [13–16]. In the IMP-SINDA project we collected normative data for the Infant Motor Profile (IMP) [15] and the Standardized Infant Neuro-Developmental Assessment (SINDA) [16]. The IMP is a standardized instrument for infants aged 3 to 18 months focusing on the quality of motor behaviour. The IMP is not only a reliable, valid and responsive instrument to measure motor development [15], but two studies indicated that IMP scores are also related to cognitive outcome at school-age [17,18]. The total IMP score forms the primary outcome parameter of the present study. The SINDA is a novel neurodevelopmental test for infants aged 6 weeks to 12 months corrected age [16]. It aims to detect neurodisability during the first year. It includes a neurological and a developmental scale. The neurological scale has high predictive power for cerebral palsy and intellectual disability [16]. The developmental scale predicts intellectual disability [16].

The aim of the present study was to evaluate on the basis of the IMP-SINDA project whether a longer duration of gestation in singleton term infants is associated with neurodevelopmental outcome in infancy. To this end we addressed the following questions: Is a longer duration of gestation in infants born after a pregnancy of 37 weeks 0 days associated with (1) a higher total IMP score and a lower prevalence of atypical total IMP scores (< 15th percentile); (2) a higher score on SINDA's neurological scale and a lower prevalence of an atypical neurological score; (3) a higher score on SINDA's developmental scale and a lower prevalence of an atypical developmental score?

2. Materials and methods

2.1. Study design

The current project is a secondary analysis of the data of the IMP-SINDA project. The IMP-SINDA project originally aimed to collect normative data for the IMP and SINDA in 1700 infants representative of the Dutch general population. To this end each infant was assessed once, implying that the study has a cross-sectional observational design.

2.2. Participants

The IMP-SINDA project included 1700 infants aged 2–18 months corrected age. Infants were recruited via well-baby clinics and advertisements. Inclusion criteria were age between 2 and 18 months, living in the northern part of the Netherlands, and having caregivers with sufficient comprehension of the Dutch language. Infants were only excluded if they were too ill to be evaluated (e.g., severe heart or muscle disease largely interfering with movement activities). According to plans we were able to recruit 100 infants per month of age and to generate a sample that was representative of the Dutch population (for details see references [12–15]). In the present study only singleton infants born after 37 weeks 0 days of gestation were included ($n = 1563$; Table 1, Fig. 1).

2.3. Study logistics

Assessments took place between January 2017 and March 2019 at the Institute of Developmental Neurology, University Medical Center Groningen, at well-baby clinics, or at the infants' homes, depending on caregivers' preferences. Each infant was assessed once. All infants had an IMP and SINDA assessment performed by a trained member of the IMP-SINDA project team. Assessments were video-taped and supervised by an expert (MHA or KRH). The assessors were not aware of the clinical history of the infants.

The caregivers filled out a standardized questionnaire on prenatal, perinatal and neonatal and socio-economic history. Pregnant women in the Netherlands know the expected date of delivery well [19]. The date is based on a dating ultrasound performed at 8–13 weeks' gestation [19]. If the standardized questionnaire revealed complications or unclearities, medical records were consulted (see Table 1 for background characteristics). The Medical Ethical Committee of the University Medical Centre in Groningen approved of the study design (METC 2016/284). Caregivers provided written informed consent.

2.4. Outcomes

The total IMP score was our primary outcome parameter. The IMP is a video-based assessment of infant motor behaviour in the age range of 3 to 18 months corrected age. It evaluates the infant's self-produced movements during standardized play. The IMP focuses in particular on the quality of movements. Its 80 items generate scores in five domains: variation (size of the motor repertoire), adaptability (ability to select an efficient strategy from the repertoire), symmetry, fluency and performance. The latter is the only non-qualitative domain, it assesses the infant's motor skills. On the basis of the domain scores a total score is computed. Raw scores are percentage scores with a maximum of 100%. Recently, IMP's norm reference values (percentile curves) have been published [15]. The IMP has valid psychometric properties, including good reliability and predictive validity: low IMP scores are associated with cerebral palsy and lower intelligence quotients at school age [15,17,18,20]. In this study we used the raw total IMP scores and the prevalence of atypical total IMP scores defined as scores below the 15th percentile (P15).

SINDA's neurological and developmental scales generated secondary outcome parameters. The neurological scale consists of 28 dichotomized items (maximum score 28) and the developmental scale has 15 dichotomized items per month (maximum score 15). SINDA has good psychometric properties, including a high predictive value for neurodisability [16]. An atypical score of the neurological scale (≤ 21 points) indicates a high risk of cerebral palsy and learning disability, that of the developmental scale (≤ 7 points) a high risk of learning disability [16]. We used the raw scores and the prevalence of atypical scores.

Table 1

Background characteristics of the 1563 Dutch singleton term infants of the IMP-SINDA project aged 2–18 months, assessed in 2017–2019.

Risk factor	37 ⁺⁰ –38 ⁺⁶ wk ^a n = 385 (24 %) ^b	39 ⁺⁰ –40 ⁺⁶ wk. n = 874 (56 %) ^b	41 ⁺⁰ –42 ⁺³ wk ^c n = 304 (20 %) ^b	37 ⁺⁰ –38 ⁺⁶ wk ^d OR [95 % CI]	41 ⁺⁰ –42 ⁺³ wk ^d OR [95 % CI]
Sex, male, n (%)	203 (53 %)	461 (53 %)	146 (48 %)	1.000 [0.893–1.121]	0.909 [0.799–1.034]
Level of maternal education, n (%) ^e					
- low	43 (11 %)	80 (9 %)	15 (5 %)		
- middle	194 (51 %)	382 (44 %)	123 (41 %)		
- high	146 (38 %)	412 (47 %)	165 (54 %)	0.854 [0.773–0.945]	1.164 [1.014–1.337]
Maternal ethnicity, non-Western ^f , n (%)	33 (9 %)	85 (10 %)	22 (7 %)	0.988 [0.951–1.025]	0.973 [0.973–1.011]
Maternal age, years, mean ± SD	30.4 ± 4.6	30.2 ± 4.3	30.5 ± 4.6		
- Advanced maternal age (≥35 yr), n (%)	77 (20 %)	141 (16 %)	64 (21 %)	1.049 [0.990–1.111]	1.062 [0.995–1.133]
Maternal nulliparity, n (%)	178 (46 %)	424 (48 %)	175 (58 %)	0.958 [0.855–1.072]	1.213 [1.049–1.404]
Maternal prepregnancy BMI, median (IQR)	24.7 (21.5–28.7)	23.6 (21.2–26.9)	23.4 (21.5–26.6)		
- Maternal overweight or obesity (BMI ≥25), n (%)	178 (46 %)	319 (36 %)	113 (37 %)	1.191 [1.071–1.325]	1.010 [0.914–1.116]
Maternal smoking pregnancy, n (%)	42 (11 %)	73 (8 %)	20 (7 %)	1.029 [0.988–1.071]	0.981 [0.946–1.017]
Maternal hypertension pregnancy, n (%)	90 (23 %)	60 (7 %)	13 (4 %)	1.216 [1.148–1.289]	0.973 [0.944–1.003]
Maternal diabetes pregnancy, n (%)	65 (17 %)	33 (4 %)	3 (1 %)	1.158 [1.105–1.214]	0.972 [0.955–0.989]
Delivery, n (%)					
- spontaneous, vaginal	145 (38 %)	580 (66 %)	170 (56 %)		
- induced, vaginal	161 (41 %)	163 (19 %)	86 (28 %)	1.766 [1.540–2.025] ^g	1.189 [1.065–1.328] ^g
- elective Caesarian section	34 (9 %)	61 (7 %)	1 (<1 %)		
- urgent Caesarian section	45 (12 %)	68 (8 %)	47 (16 %)		
Small-for-gestational age (<P10), n (%)	42 (11 %)	85 (10 %)	25 (8 %)	1.013 [0.972–1.056]	0.984 [0.945–1.024]
Non-optimal start after birth, n (%)	41 (11 %)	50 (6 %)	27 (9 %)	1.055 [1.016–1.097]	1.035 [0.995–1.075]
Admission to neonatal ward ^h , n (%)	100 (26 %)	136 (16 %)	51 (17 %)	1.142 [1.069–1.219]	1.015 [0.957–1.075]
Jaundice requiring phototherapy, n (%)	19 (5 %)	9 (1 %)	2 (1 %)	1.041 [1.017–1.066]	0.996 [0.985–1.008]
Age at IMP-SINDA assessment (months)	9.54 ± 4.91	10.21 ± 4.91	10.03 ± 4.99	Mean difference –0.673 [–0.084 to –1.262]	Mean difference –0.183 [–0.827–0.461]

BMI = body mass index; P10 = tenth percentile; IQR = interquartile range; SD = standard deviation; wk. = week.

Missing data: Maternal education n = 3; maternal ethnicity n = 1; maternal age n = 2; maternal BMI n = 5; maternal smoking n = 1; maternal hypertension n = 2; maternal diabetes n = 1; mode of delivery n = 2; small-for-gestational-age n = 2; non-optimal start n = 3; admission to neonatal ward n = 1.

^a Including n = 131 born at 37 weeks (37⁺⁰–37⁺⁶);^b % of entire group of IMP-SINDA term singletons (n = 1563);^c Including n = 23 infants born post-term (42⁺⁰–42⁺³ weeks);^d Full-term, i.e., 39⁺⁰–40⁺⁶ weeks as reference;^e Levels of education: low: only primary education or primary vocational education; middle: secondary vocational training, senior general secondary education, university preparatory education; high: vocational college, university; OR calculated for high maternal education;^f Non-Western, e.g. originating from Turkey, Syria, Morocco, Somalia, Nigeria and Indonesia.^g OR calculated for no spontaneous vaginal delivery.^h The reasons for admission to the neonatal ward were heterogeneous, with the most prevalent causes being jaundice requiring phototherapy (see Table), respiratory distress (37–38 wk.: n = 12 (3 %); 39–40 wk.: n = 6 (0.7 %); 41–42 wk.: n = 5 (2 %)); observation due to (a) maternal diabetes (37–38 wk.: n = 6 (2 %)); 39–40 wk.: n = 11 (1 %); 41–42 wk.: n = 5 (2 %)); (b) suspicion of infection / premature rupture of membranes (37–38 wk.: n = 12 (3 %); 39–40 wk.: n = 15 (2 %); 41–42 wk.: n = 4 (1 %)); (c) perinatal complications (37–38 wk.: n = 8 (2 %); 39–40 wk.: n = 14 (2 %); 41–42 wk.: n = 9 (3 %)); and (d) SGA (37–38 wk.: n = 6 (2 %); 39–40 wk.: n = 5 (0.6 %); 41–42 wk.: n = 1 (0.3 %)).

2.5. Statistical analysis

Power calculation was based on our primary outcome measure, the total IMP score. Previous publications indicated that two groups of 16 infants would yield a power of 80 % ($\alpha = 0.05$) to detect a difference of 1 standard deviation (6 points) [21].

To estimate the differences in background variables and atypical outcomes between the infants born at various gestational ages we calculated the Odds Ratios (OR) with 95 % confidence intervals (CI) using infants born at 39–40 weeks as a reference group. In the analyses of the effect of various gestational ages on atypical outcomes we used logistic regression analyses in which we corrected for the set of

confounders listed in the next paragraph. We used a backward stepwise elimination procedure to reach best model fit without losing factors that did not contribute to the model. These analyses were performed using the IBM Statistical Package for the Social Sciences 23.0 for Windows.

Our analysis focussed on the effect of the duration of gestation on the neurodevelopmental outcome parameters using multivariable linear and logistic regression models. In the analyses we took into account the effect of potential maternal confounders (maternal education, ethnicity, age, body mass index (BMI), smoking, hypertension, diabetes, nulliparity). Additionally, we included the following covariates: infant sex, mode of delivery, being small-for-gestational-age, non-optimal start at birth, neonatal ward admission, jaundice requiring phototherapy and

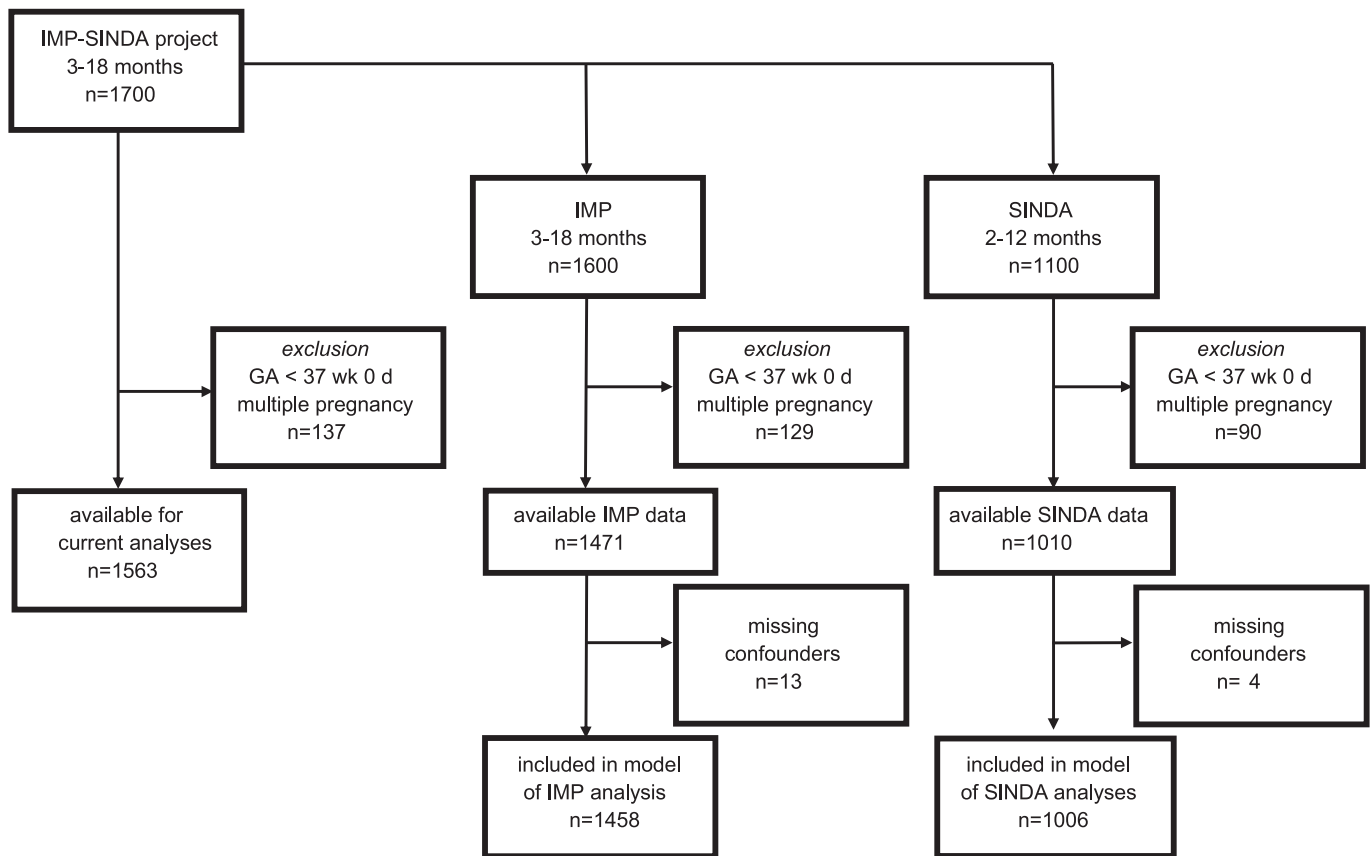


Fig. 1. Flow diagram: Selection of term infants from the IMP-SINDA project for the current study and availability of IMP and SINDA data.

infant age at the neurodevelopmental assessment. We corrected a priori for all confounders and covariates mentioned, including quadratic age at assessment for the IMP score analyses, as previous research showed the existence of a quadratic relationship between age and IMP [15]. For the IMP analyses, data of infants aged at least 3 months were included ($n = 1458$); for the SINDA analyses, data of infants aged 2 to 12 months were used ($n = 1006$). Each model was optimized for model fit using potential linear, quadratic and cubic gestational age to arrive at best fitting curvature for describing the relationship between gestational age and outcome.

From the resulting models best describing the (potentially curved) effect of gestational age on outcome (linear regression models) or predicted probability on adverse outcome (logistic regression models), the average effect of duration of gestation in the range of 37 weeks and 0 days to 42 weeks and 3 days weeks on each outcome was plotted for a 10-months-old (IMP scores) or a 7-months-old (SINDA) infant (with all covariates fixed at reference value 0). The multivariable linear and logistic regression were performed using R, version 3.6.3 [22].

3. Results

3.1. Background characteristics

Table 1 shows the associations between social, prenatal, perinatal and neonatal characteristics and duration of gestation. A longer duration of gestation was associated with a higher prevalence of high maternal education and a lower prevalence of maternal diabetes and non-spontaneous vaginal delivery (Table 1). Nulliparity occurred more often in pregnancies that had lasted 41 to 42 weeks. In addition, pregnancies that lasted 37 to 38 weeks had been more often complicated by maternal overweight or obesity, maternal hypertension, a non-optimal start of the infant at birth, admission of the infant to the neonatal

ward and jaundice requiring phototherapy than pregnancies lasting 39 to 40 weeks (Table 1). Moreover, the age at assessment of the infants born at 37–38 weeks was on average 0.66 months less than that of the infants born at 39–40 weeks (Table 1).

3.2. Neurodevelopmental outcome

Fig. 2a depicts the association between gestational age at birth and total IMP scores. The final model included quadratic gestational age, i.e., duration of gestation had a curved relationship with the total IMP score with a minimum for the estimated average IMP score (just below 91) at a duration of gestation of 38.5 weeks. A similar quadratic relationship of the duration of gestation was found for the prevalence of atypical IMP scores (Fig. 2b). The model showed that the highest prevalence of atypical IMP scores occurred between 37.9 and 38.1 weeks of gestation. Comparison of the infants born at 41 to 42 weeks of gestation with those born at 39 to 40 weeks indicated that the former had significantly less often atypical IMP scores than the latter (adjusted OR [95 % CI]: 0.571 [0.341 to 0.957] (Table 2).

Duration of gestation was not associated with SINDA's neurological scale score nor with the prevalence of atypical neurological scores when confounders and co-variables were taken into account (Table 2). On the other hand, duration of gestation was associated with SINDA's developmental scale score: again the relation was quadratic (Fig. 2c). The lowest point in the curve (a score just below 10) was found at a gestational age of 38.7 weeks. Duration of gestation also had a quadratic relationship with atypical developmental scores: the highest prevalence of atypical developmental scores occurred at 38.8 weeks. Comparison of the infants born at 41 to 42 weeks of gestation with those born at 39 to 40 weeks showed that the former had significantly less often atypical developmental scores than the latter (adjusted OR: 0.66 [0.195 to 0.688]) (Table 2).

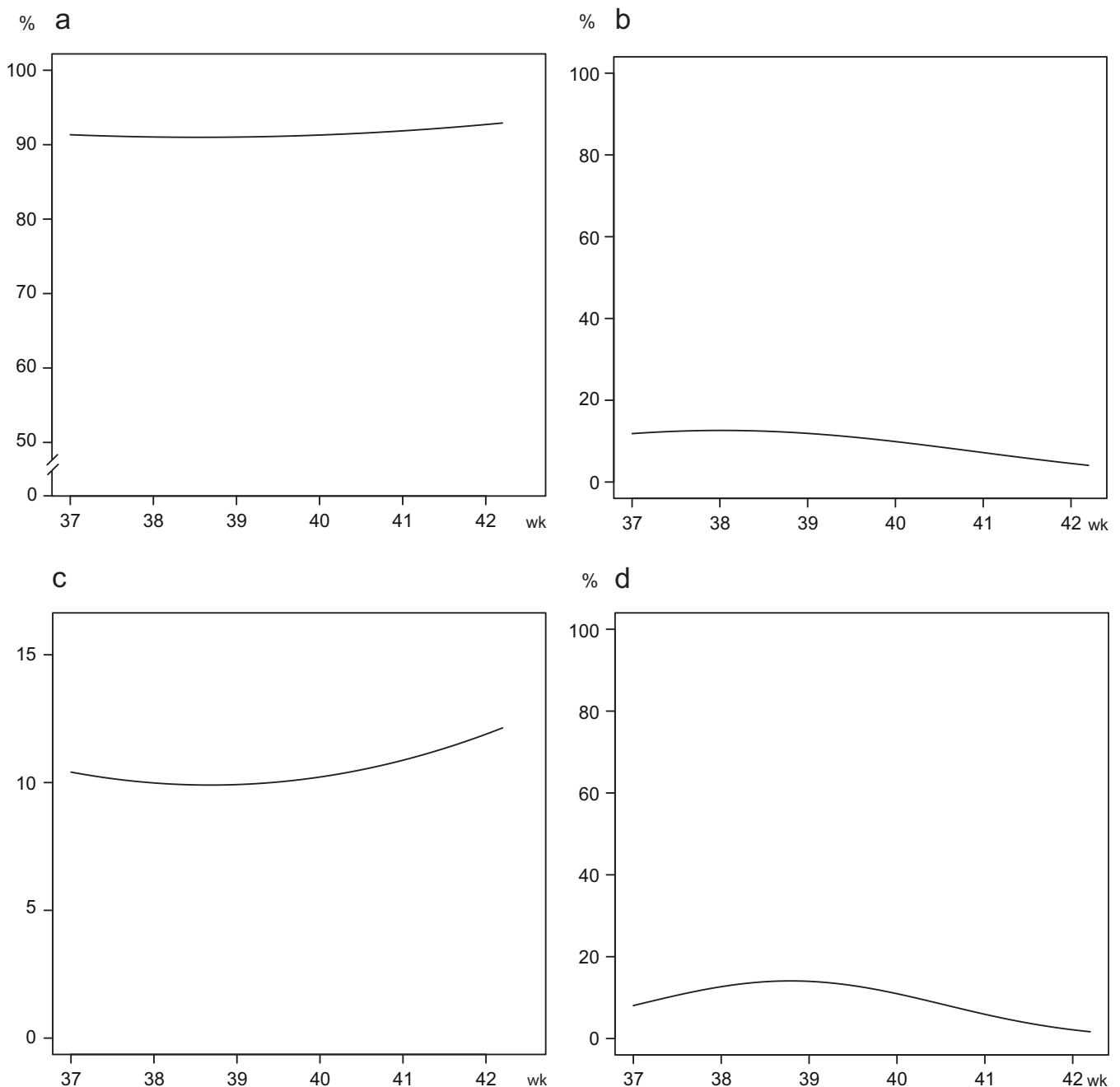


Fig. 2. Estimated average neurodevelopmental outcomes of infants born in the gestational age range of 37 + 0 to 42 + 3 weeks: a) total IMP scores; b) prevalence of atypical total IMP scores (<P15); c) SINDA developmental scores; d) prevalence of atypical developmental scores (≤ 7 points). The IMP-plots depict the effect of gestational age (x-axis) on IMP-score (y-axis) as described by the best fitting model (here for an average infant aged 10 months); the SINDA-plots depict the effect of gestational age (x-axis) on SINDA-score (y-axis) as described by the best fitting model (here for an average infants aged 7 months).

4. Discussion

This cross-sectional observational study in a group of recently born infants representative of the Dutch population indicated that a longer duration of gestation in singleton term infants was associated with better IMP and SINDA developmental scores. As a result a longer gestation also resulted in a lower prevalence of infants with atypical scores. A longer duration of gestation in term infants was not associated with a higher prevalence of atypical neurological scores.

Our results generate two messages. First, the finding that duration of gestation was not associated with an increase in infants with atypical neurological scores, indicates that in term singletons duration of

gestation does not affect the risk of neurodisability, including cerebral palsy [16]. This may imply that our finding differs from that of Figlio and colleagues, who reported that children born at 41 weeks of gestation had a higher risk of physical disability than children born at 39 and 40 weeks [9]. The difference may be attributed to differences in (a) age at assessment (infancy versus school-age) and (b) definition of the outcome measure: at high risk of neurodisability assessed with a standardized assessment versus physical disability (an orthopaedic, speech or sensory impairment or being hospitalbound or homebound) observed in the child's medical record at school. This means that future studies need to address the effect of longer gestation in term singleton infants on neurodisability.

Table 2

Prevalence of atypical neurodevelopmental scores in early term, full term and late-to-post-term infants of the Dutch IMP-SINDA project.

	Early term	Term	Late-to-post-term	37 ⁺⁰ –38 ⁺⁶ wk ^a		41 ⁺⁰ –42 ⁺³ wk ^{a,b}	
	37 ⁺⁰ –38 ⁺⁶ wk, n (%)	39 ⁺⁰ –40 ⁺⁶ wk, n (%)	41 ⁺⁰ –42 ⁺³ wk, n (%)	unadj OR [95 % CI]	adj OR [95 % CI]	unadj OR [95 % CI]	adj OR [95 % CI]
IMP, infants 3–18 months							
Number of infants	366	826	279				
Atypical total IMP score < P15	62 (17 %)	96 (12 %)	19 (7 %)	1.556 [1.101–2.200]	1.379 [0.959–1.984]	0.556 [0.333–0.927]	0.571 [0.341–0.957]
SINDA, infants 2–12 months							
Number of infants	258	554	198				
Atypical neurological score (≤21)	25 (10 %)	29 (5 %)	11 (6 %)	1.926 [1.104–3.360]	1.691 [0.920–3.105]	1.065 [0.522–2.174]	0.987 [0.477–2.042]
Atypical develop. Score (≤7)	49 (19 %)	86 (16 %)	12 (6 %)	1.288 [0.875–1.897]	1.226 [0.808–1.862]	0.355 [0.189–0.665]	0.366 [0.195–0.688]

unadj OR = unadjusted Odds Ratio; adj OR = adjusted Odds Ratio taking into account the following confounders: maternal education, maternal overweight or obesity, nulliparity, maternal hypertension, maternal diabetes, urgent Caesarian section. In addition, the role of the following co-variables was taken into account: non-optimal start after delivery, admission to neonatal ward, jaundice needing phototherapy and infant age at neurodevelopmental assessment (in line with Table 1).

^a Full-term, i.e., 39⁺⁰–40⁺⁶ weeks as reference; early term = 37⁺⁰–38⁺⁶ weeks; late term = 41⁺⁰–41⁺⁶ weeks; post-term = ≥ 42⁺⁰ weeks [5].

^b Exclusion of the infants born at ≥42⁺⁰ weeks of gestation only minimally changed the results.

Second, in our group a longer gestation was associated with better IMP and SINDA developmental scores. Here it is important to realize that in our group only a small proportion of children had been delivered at post-term age (≥ 42⁺⁰ weeks; Table 1). This corresponds to the Dutch guidelines to offer pregnant women in week 41 the option of induction of labour [23]. It is possible, as the review of Glover Williams and Odd [12] indicated, that a gestation of 42 weeks or more is associated with less favourable neurodevelopmental outcome. In other words, it is conceivable that for the child's neurodevelopmental outcome a gestation of 41 weeks is optimal. The data suggest that a longer gestation at term age up to and including 41 weeks of gestation is associated with more efficient brain networks, as IMP and SINDA developmental scores predict intellectual functioning in childhood [15,16]. This means that our findings on how infants function in everyday tasks correspond to earlier reports that longer gestation at term age up to and including 41 weeks of gestation is associated with more favourable brain morphometry [10] and neural network efficiency [11]. Our findings correspond to those in earlier birth cohorts reporting an association between longer gestation up to and including 41 weeks of gestation and better cognitive performance at school age [8,9]. Another study on term children born about a decade ago in China reported that children delivered at 37 weeks had lower cognitive scores in infancy than children born at 39–41 weeks, but that a similar effect of gestational age was absent at preschool age [24]. This contrasting finding may be explained by the well-known hardship to document perinatal-developmental relationships at preschool age. Often these relationships can be established in infancy and at school-age but not at preschool age [25].

The association between longer gestation at term age up to and including 41 weeks of gestation and better neurodevelopmental scores may be based on underlying associations induced by, for instance, genetic effects or maternal psychological stress. Maternal genetic effects have been associated with a longer duration of gestation and may predispose to better infant outcome [26]. Maternal psychological stress during pregnancy is associated with reduced placental quality and reduced foetal weight, which may result in earlier infant delivery, and a less favourable neurodevelopmental outcome of the infant [27,28]. Nonetheless, also a direct effect is conceivable. A longer intrauterine stay during a period with peaking developmental activity in the brain [29] may facilitate the formation of optimal neural networks. A longer stay in utero does not only provide a longer stay in the environment that is optimal for the majority of foetuses, but it also postpones the foetus' physiologically challenging transition from intrauterine to extrauterine life. A longer intrauterine stay may allow the foetal body and brain more preparatory time for the adjustments facilitating an optimal transition.

Knowledge that a longer duration of gestation at term age is associated with better neurocognitive outcome makes obstetrics not easier, as it is also known that a longer duration of pregnancy increases the risk of perinatal mortality [3,4]. Thus, the art of obstetrics is to balance in each woman with a term singleton pregnancy up to and including 41 weeks of gestation the two conflicting effects of a longer duration of gestation, i.e., the increasing risk of perinatal death [3,4] and the increasing chance of a better neurocognitive outcome. Currently, obstetrical decision making is mainly based on maternal outcomes and the risk of perinatal mortality. In recent years this has induced a global increase in the rate of elective caesarean sections, the majority occurring at term age [30,31]. The current findings stress the need to consider in the timing of the infant's term birth also the effect of longer gestation up to and including 41 weeks of gestation on the child's neurocognitive outcome.

The study's strengths are the nature of the study group consisting of a sample of term singletons representative of the Dutch population and the use of well validated and standardized infant tests. The strength of the representativeness of the Dutch population is also associated with a limitation: due to the implementation of obstetric guidelines in Dutch daily practice our study included few post-term babies, therewith precluding a conclusion on the effect of post-term gestational age on neurodevelopmental outcome. The age at the neurodevelopmental assessments is another limitation of the study, as infant age precludes the assessment of intelligence quotients as a well-known proxy of brain network efficiency. Other limitations are the study's cross-sectional design and the absence of neuroimaging data.

In conclusion: our cross-sectional and observational study in term singleton infants representative of the Dutch population indicates that a longer duration of gestation up to and including 41 weeks of gestation is associated with better infant neurodevelopment. The study also showed that duration of gestation at term age is not associated with atypical neurological scores, suggesting an absent association with neurodisability, such as cerebral palsy.

We suggest that future research replicates our study and combines infant neurodevelopmental assessments with long-term follow-up that does not only include the evaluation of cognitive function at school age and adult age, but also – in representative subgroups – neuroimaging. Future studies need to pay special attention to the association between gestational age and neurodisability.

Declaration of competing interest

None declared.

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CRedit authorship contribution statement

MHA and KRH initiated and supervised the data collection of the IMP-SINDA project.

MHA and PAMvI initiated the current study. MHA, PAMvI and SIBvG performed the data analysis. MHA wrote the draft paper, all authors commented on the draft and approved the final version.

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