Gestational age at birth and sleep duration in early childhood in three population-based cohorts

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ABSTRACT

Background: Both preterm and post-term births have been associated with neonatal morbidity and mortality, including adverse impact on neurodevelopment. Important neural maturational processes take place during sleep in newborns, but findings on gestational duration and sleep in early childhood are contradictory and often derive from small clinical samples. We studied the association of gestational age at birth with sleep duration in early childhood in three population-based cohorts.

Methods: Gestational age at birth and sleep duration were assessed in three population-based cohort studies in The Netherlands (n = 6471), Singapore (n = 862), and Canada (n = 583). Gestational age at birth was assessed using ultrasound in pregnancy in combination with date of birth, and caregivers repeatedly reported on child sleep duration at three, six, 24, and 36 months of age. Generalized estimating equations were used, which were adjusted for confounders, and findings were pooled in a meta-analysis.

Results: Children born preterm (<37 weeks of gestation) showed longer sleep duration than children born at term; and children born post-term (≥42 weeks of gestation) showed shorter sleep duration. The meta-analysis indicated a small negative effect of gestational age on child sleep duration (effect size −0.11), when assessed in children born at term only.

Conclusion: In early childhood, children with a lower gestational age have a longer sleep duration, even when they are born at term (37−42 weeks of gestation). These subtle yet consistent findings point to the importance of maturational processes during sleep, not only in premature children but also in children born at term after shorter gestational duration.

1. Introduction

Timely onset of labour is important for perinatal and postnatal health. Both preterm (<37 weeks of gestation) and post-term (≥42 weeks of gestation) births have been associated with neonatal

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morbidity and mortality, including adverse impact on neurodevelopment [1−3]. Although sleep is crucial for the development of neural networks [4], and preterm birth affects the neural network that regulates sleep architecture [5], effects of gestational age at birth on postnatal sleep have not been well studied [6]. Moreover, findings have been contradictory. Some studies report more sleep problems and a shorter sleep duration in premature infants [7] and also after the first months of life [8]; while others report no differences in sleep duration between preterm and term infants [9,10] or longer sleep duration in preterm infants [11,12]. Environmental and physiological mechanisms that might explain these contradictory effects are still unclear [6].

Sleep is critical for maturation in all areas of child development [13]. Current knowledge on the effects of gestational age at birth on sleep derives largely from clinical samples with (very) premature infants. Sample sizes are often small, and only a handful of studies used longitudinal designs. Furthermore, both obstetrician policy [1] and sleep habits differ among cultures [14], limiting the generalizability of available studies, mainly conducted in individuals of Caucasian/white ethnicity. In this study, using data from three population-based prospective cohorts across different continents, we explored the association of gestational age at birth and sleep duration in early childhood in the general population.

2. Methods

2.1. Study population

This study was conducted in three cohorts: the Generation R Study [15] (n = 6471; inclusion started in 2002 in The Netherlands); the Growing up in Singapore Towards healthy Outcomes cohort [16] (GUSTO, n = 862; inclusion started in 2009 in Singapore); and the Maternal Adversity, Vulnerability And Neurodevelopmental cohort [17] (MAVAN, n = 581; inclusion started in 2003 in Canada). The three study populations consist of children with information on gestational age at birth and sleep data at three, six, 24, and 36 months of age.

2.2. Gestational age at birth

Ultrasound measurements in early pregnancy (the Generation R Study) and early to mid-pregnancy (GUSTO, MAVAN) were used to determine gestational age to the nearest day in combination with date of birth [15−17]. Preterm birth was defined as birth before 37 weeks gestation, term birth between 37 and 42 weeks gestation, and post-term birth after 42 weeks gestation.

2.3. Sleep assessments

In the all three cohorts, bedtimes, wake times and nap duration were reported by parents [15,17,18]. Questions were derived from The Brief Infant Sleep Questionnaire (BISQ [19]), and include 'How much time (on average) does your child spend in sleep during the night?' and 'How much time (on average) does your child spend in sleep (naps) during the day?'. Total sleep duration was calculated as hours of sleep per 24 h by adding nighttime and daytime sleep. Sleep duration was reported at ages three, six, 24, and 36 months; correlations between sleep duration at the four time points varied from $r = 0.42$ to 0.04 (time points closest to each other showed the highest correlations).

2.4. Statistical analyses

Although we had data at each of the time points, we combined all information using generalized estimating equations (GEE) to analyse the relation of gestational age at birth with sleep duration at four time points in three cohorts. With GEE analyses, symptoms repeatedly measured over time can be analyzed, taking into account that these repeated measurements within the same subject are correlated. Next, we compared the groups of preterm and post-term children, using term born children as the reference category (only in the Generation R Study; numbers in the other cohorts were too small: in MAVAN, $n < 10$ for preterm and post-term born children; in GUSTO, $n = 0$ for post-term born children). To test for effects of conceptional age, analyses were rerun including only term born children. If main effects were significant, time effects and gestational age × time interactions were tested.

All models (in all cohorts) were adjusted for potential confounders; birth weight and gender of the child, time points of sleep assessments, maternal age and education, and maternal smoking and drinking during pregnancy. In the Generation R Study and GUSTO, analyses were additionally adjusted for maternal ethnicity. Sleep duration was calculated in hours, with effect size B indicating the change in sleep duration per standard deviation change in gestational age. The mean proportion of missing values for confounders was 8.2%, 1.6%, and 8.0% in the Generation R, GUSTO, and MAVAN cohort, respectively, and multiple imputation was performed in 10 datasets. Only confounder variables were imputed. Finally, we performed a meta-analysis with a fixed-effects model (tests of heterogeneity indicated that samples were not heterogeneous).

3. Results

3.1. Gestational age and sleep duration in the three cohorts

Descriptive statistics for the three cohorts are presented in Table 1. Sleep duration for all ages and all cohorts can be found in Table 2. In the Generation R cohort, gestational age at birth was negatively related to total sleep duration (B = −0.13; 95% confidence interval [CI]: −0.18 to −0.07; $p < 0.001$), night sleep duration (B = −0.06; 95% CI: −0.10 to −0.03; $p < 0.001$), and nap duration (B = −0.03; 95% CI = −0.06 to −0.01; $p < 0.017$), indicating that children with lower gestational age sleep longer. A categorical approach showed similar results: preterm children were more likely to have longer sleep duration compared to term children (B = 0.26; 95% CI: 0.09 to 0.42; $p = 0.003$), whereas post-term children were more likely to have shorter sleep duration compared to term children (B = −0.15; 95% CI: −0.28 to −0.03; $p = 0.019$). When analyses were restricted to term born children (37−42 weeks of gestation) to address the potential effect of conceptional age, the association remained.

A time effect was present; total sleep time and nap duration decreased as children grew older, whereas night sleep increased with age (data not shown). An interaction effect of gestational age × time was present (B = 0.03; 95% CI: −0.00 to −0.06; $p = 0.036$). Individual time points indicated that children born after shorter gestational duration slept longer at ages three and six months, but not at ages 24 and 36 months (data not shown). However, no interaction was found when restricting the sample to term children, suggesting that the effect was driven mainly by preterm children.

Analyses in the GUSTO cohort showed that gestational age was not associated with total sleep duration (B = −0.07; 95% CI: −0.24 to 0.11; $p = 0.46$), night sleep duration (B = −0.07; 95% CI: −0.24 to −0.11; $p = 0.46$), or nap duration (B = 0.07; 95% CI: −0.39 to 0.53; $p = 0.77$).

In the MAVAN cohort, no significant associations were observed between gestational age and total sleep (B = −0.04; 95% CI: −0.15 to 0.07; $p = 0.46$), night sleep (B = 0.01; 95% CI: −0.07 to 0.10; $p = 0.75$), or nap duration (B = −0.05; 95% CI: −0.13 to 0.02; $p = 0.13$).

Table 1
Demographic information of the three study populations.

	Generation R Study (n = 5637)	GUSTO (n = 862)	MAVAN (n = 581)
Maternal characteristics			
Maternal age at intake, y	30.8 ± 0.06	30. 7 ± 0.17	30.7 ± 0.20
Educational level			
Primary education (%)	8.4	4.2	–
Secondary education (%)	41.4	25.1	–
Higher education (%)	50.2	–	–
High school or less (%)	–	–	9.8
Some community college (%)	–	–	9.0
Complete community college (%)	–	–	32.4
University degree (%)	–	–	48.8
Post-secondary education (%)	–	11.5	–
General certificate of education (GCE) (%)	–	25.9	–
University (%)	–	33.3	–
Maternal ethnicity			
Dutch (%)	57.5	–	–
Non-Dutch western (%)	8.6	–	–
Non-Dutch non-western (%)	33.9	–	–
Canadian	–	–	100
Chinese (%)	–	55.7	–
Malay (%)	–	26.6	–
Indian (%)	–	17.6	–
Other (%)	–	0.1	–
Smoking habits			
Never smoked in pregnancy (%)	72.5	97.6	80.3
Smoked in pregnancy (%)	–	2.4	–
Smoked in early pregnancy (%)	13.0	–	9.8
Smoked throughout pregnancy (%)	14.5	–	9.9
Drinking habits			
Never drank in pregnancy (%)	38.8	97.6	59.4
Drank during pregnancy (%)	–	2.4	40.6
During early pregnancy (%)	17.8	–	–
Throughout pregnancy, occasionally (%)	34.5	–	–
Throughout pregnancy, frequently (%)	8.9	–	–
Child characteristics at birth			
Sex of the child (% male)	50.2	52.8	54.4
Birth weight, g	3422 ± 7.1	3097 ± 14.7	3376 ± 18.9
Gestational age at birth, wk	39.8 ± 0.02	38.4 ± 0.05	39.5 ± 0.05
Range	25.3–43.4	25.0–41.0	36.7–42.1
Timing of birth			
Term	87.1	93.2	98.1
Preterm	5.8	6.8	0.9
Post-term	7.1	–	1.0
Mode of delivery (%)			
Vaginal delivery	70.5	65.0	–
Assisted vaginal delivery (forceps/vacuum)	17.3	4.7	–
Cesarian delivery	12.2	30.8	–
Apgar scores at birth			
Apgar <7 at 1 min (%)	5.4	2.6	6.4
Apgar <7 at 5 min (%)	1.0	–	1.2

All continuous variables are presented as means ± standard error; all categorical variables are presented as percentages.

[a]p Values are derived from analyses of variance for parametric continuous variables, Kruskal–Wallis tests for nonparametric continuous variables, and χ^2.tests for categorical variables with the term born children as the reference group.

3.2. Meta-analytic pooling

We performed meta-analyses to pool the effects for total sleep, night sleep, and nap duration across the three cohorts. Gestational age at birth was associated with total sleep duration (B_{pooled} = −0.11, 95% CI: −0.15 to −0.06), night sleep duration (B_{pooled} = −0.05, 95% CI: −0.08 to −0.02), and nap duration (B_{pooled} = −0.04, 95% CI: −0.06 to −0.01). When restricting the analyses to term children, the associations remained (Fig. 1).

4. Discussion

Our study demonstrated that children born after shorter gestational duration slept longer than their term born peers. Moreover, the longer the gestational duration, the shorter children slept. The direction of effects aligned over three prospective cohort studies, even after controlling for confounders (such as birth weight) and also when tested in term born children only (37–42 weeks of gestation). Findings from the Generation R Study suggested that the association between gestational age and sleep duration is most prominent in the first year of life.

These results partly converge with those of earlier studies; some studies report shorter sleep [7,8], some longer sleep [11,12], and some no differences [9,10]. Most studies used clinical samples (children born at <32 weeks of gestation, low birth weight), and study samples rarely exceed 200 participants, limiting the power to detect small effects. No studies tested the effects of gestational duration in term born children only, or in children born post-term.

Our findings point to the importance of maturational processes during sleep, not only in premature children but also in children born at term after shorter gestational duration. In early childhood, sleep is a state involving maturation of the central nervous system

Table 2
Total sleep duration in hours per day in the three cohorts.

	Generation R Study	GUSTO	MAVAN
3 Months			
Mean ± SD	14.6 ± 3.0	12.5 ± 3.5	14.2 ± 2.5
Range	6.0–22.0	6.0–22.0	7.0–21.0
n	4800	537	170
% below recommendation (<12 h)[a]	15.2	41.7	12.9
6 Months			
Mean ± SD	15.0 ± 2.7	12.1 ± 2.5	13.2 ± 1.9
Range	6.0–21.0	6.0–21.0	7.0–21.0
n	3691	647	483
% below recommendation (<12 h)[a]	11.3	42.0	20.3
24 Months			
Mean ± SD	13.4 ± 1.1	11.3 ± 1.4	12.5 ± 1.2
Range	6.4–19.0	6.5–19.0	8.0–16.5
n	5114	374	425
% below recommendation (<11 h)[a]	2.1	30.7	8.0
36 Months			
Mean ± SD	12.6 ± 1.2	11.0 ± 1.5	11.8 ± 1.2
Range	8.5–20.0	6.5–20.0	7.5–15.0
n	4847	170	409
% below recommendation (<10 h)[a]	0.4	10.6	4.9

Children with unreliable estimates of sleep duration (<6 h of sleep at all ages and maximum sleep duration of 22, 21 and 24 h at the age of three months, six months and 24/36 months) were excluded from the analyses.

SD, standard deviation.

[a] Guidelines from the American Academy of Pediatrics (AAP) recommend the following ranges of sleep duration: infants 4–12 months of age: 12–16 h per 24 h (including naps); children 1–2 y of age: 11–14 h per 24 h (including naps); children 3–5 y of age: 10–13 h per 24 h (including naps).
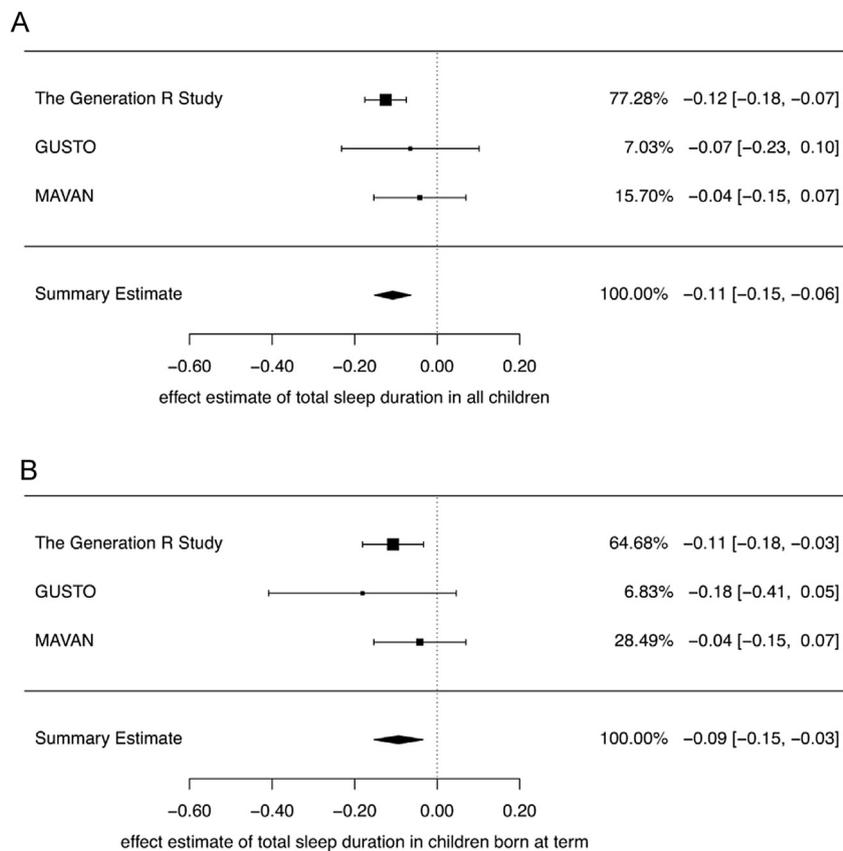
Fig. 1. Forest plot of effects of gestational age on sleep duration in early childhood in three population-based cohorts. (A) All children. (B) Term children only.

[20], and children might progress on maturational processes, such as neural network connectivity, predominantly during sleep [4,21]. Our findings in post-term children in the Generation R Study point in the same direction: compared to their term born counterparts, children born post-term showed shorter sleep duration. Furthermore, results from the Generation R Study suggest that the effect of gestational age on sleep might be most pronounced in the first year of the child's life, particularly in preterm children. Catch-up in

many developmental areas in the first year of life is common for children born preterm [3], and rapid catch-up has been suggested to predict better neurodevelopmental outcomes [22].

This study has multiple strengths. We were able to use repeated assessments from three large cohort studies from different continents, increasing power to find small effects, and increasing generalizability of findings to other populations. Differences in continents, ethnicities, and socio-economic backgrounds have been associated with differences in gestational age and sleep duration [18]. Indeed, in the current study, children from Singapore showed somewhat shorter sleep duration; parental beliefs about sleep may differ across cultures, which in turn may influence child sleep [14]. However, even when controlled for ethnic and demographic confounders, we found a small consistent effect across the cohorts.

Some study limitations should also be considered. Although the findings from the different cohorts align, significant findings were found only in one of the cohorts. The pooled effect size is small, which may limit clinical impact. With the current design, we were not able to assess whether differences in sleep duration may affect other developmental outcomes. Second, due to differences in local obstetrician policy and study design, we were able to study post-term birth only in the Generation R Study. Labour induction before 42 weeks of gestation has increased, but post-term births still occur (up to 5–10%) [1]. Third, the current study made use of caregiver reports of child sleep duration, and did not assess child sleep duration objectively. Ideally, sleep quantity, quality, and chronotype would be assessed with actigraphy or polysomnography [6].

5. Conclusion

In conclusion, meta-analytically pooled evidence from three international cohorts showed that children born after shorter gestational duration slept longer, even when they were born at term. Findings from the Generation R Study suggested catch-up sleep of preterm children in the first year of life. Further research is needed to determine how sleep duration and sleep quality early in life are related to neurodevelopmental outcomes, and which environmental, physiological, and (epi)genetic factors contribute to susceptibilities in child sleep architecture.

Conflict of interest

All authors have no conflict of interest to declare. There was no external grant or financial support for this study.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleepx.2019.100002.

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