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Development of sleep-wake rhythms during the first year of age

E. Juulia Paavonen^{1,2} | Isabel Morales-Muñoz^{1,3} | Pirjo Pölkki⁴ | Tiina Paunio^{1,5} | Tarja Porkka-Heiskanen⁶ | Anneli Kylliäinen⁷ | Timo Partonen¹ | Outi Saarenpää-Heikkilä^{8,9}

Correspondence

E. Juulia Paavonen, Department of Public Health Solutions, National Institute for Health and Welfare, PO Box 30, 00271 Helsinki, Finland.

E-mail: juulia.paavonen@helsinki.fi

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Abstract

Circadian rhythms refer to biological rhythms that have an endogenous period length of approximately 24 hr. However, not much is known about the variance in the development of the sleep-wake rhythm. The study objectives were (a) to describe the normative variation in the development of a sleep-wake rhythm in infancy, (b) to assess whether slower development is related to sleep quality and (c) to evaluate factors that are related to the slower development of a sleep-wake rhythm. The study is based on a representative birth cohort. Questionnaires at the ages of 3 (n = 1,427) and 8 months (n = 1,302) and actigraph measurement at 8 months (n = 372) were available. Infants with significant developmental delays (n = 11) were excluded. The results are based on statistical testing and multivariate modelling. We found that the average percentage of daytime sleep was 36.3% (standard deviation [SD], 8.5%) at 3 months and 25.6% (SD, 6.6%) at 8 months. At both time-points, infants with slower sleep-wake rhythm development slept more hours per day, had a later sleep-wake rhythm, more difficulties in settling to sleep and longer sleep-onset latency; they also spent a longer time awake during the night. According to actigraph registrations, we found that the infants with slow development of a sleep-wake rhythm slept less and had a later start and end to night-time sleep than the other infants. Infants' sleep-wake rhythm development is highly variable and is related to parent-reported and objectively measured sleep quality and quantity. Interventions to improve the sleep-wake rhythm might improve sleep quality in these infants.

KEYWORDS

infant, sleep, sleep-wake rhythms

¹Department of Public Health Solutions, National Institute for Health and Welfare. Helsinki. Finland

²Pediatric Research Center, Child Psychiatry, University of Helsinki and Helsinki University Hospital, Helsinki, Finland

³Institute for Mental Health, School of Psychology, University of Birmingham, Birmingham, UK

⁴Department of Social Sciences, University of Eastern Finland, Kuopio, Finland

⁵Psychiatry, University of Helsinki and Helsinki University Hospital, Helsinki, Finland

⁶Physiology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland

⁷Psychology, Faculty of Social Sciences, Tampere University, Tampere, Finland

⁸Department of Paediatrics, Tampere University Hospital, Tampere, Finland

⁹Tampere Centre for Child Health Research, Tampere University, Tampere, Finland



1 | INTRODUCTION

Humans display various types of rhythms, with an endogenous period length of approximately 24 hr, among which the rest-activity rhythm is of major importance (Turek, Dugovic, & Zee, 2001). The human circadian system is driven by the circadian clock in the suprachiasmatic nucleus and is sensitive to environmental factors in midpregnancy, although it is much longer before infants start to display mature sleep-wake rhythms (Rivkees, 2007). This gradual development starts after birth and by the age of 2 months there are clear signs of circadian rhythmicity regarding both the sleep-wake cycle and hormone secretion. After the first months of life, the longest sleep periods start to accumulate in the night-time, whereas daytime sleep begins to diminish. Consequently, by the age of 3-4 months infants are usually more awake during the daytime than at night (Rivkees, 2003). The development in diurnal rhythm parallels the consolidation of night-time sleep; in other words, improvement in the quality of night-time sleep (Henderson, France, & Blampied, 2011).

The developing diurnal sleep-wake rhythm has been described previously in a questionnaire-based study by reporting the night-day ratio (Sadeh, Mindell, Luedtke, & Wiegand, 2009). This study showed that the proportion of night-time sleep increases from 60% at 0-2 months old to 70% at 3-5 months old and 75% at 9-11 months old, up to 78% at 2 years old. Slightly higher percentages of nocturnal sleep have been observed using polysomnography: infants were reported to sleep on average 78% at night at the age of 3 months, 81% at 9 months and 84% at 2 years (Louis, Cannard, Bastuji, & Challamel, 1997). There is, however, large variability in the development of diurnal sleep-wake rhythms. Some infants may already have clear day-night differences soon after birth, whereas others exhibit such rhythms much later (Rivkees, 2003). However, not much is known about the variance in the development of the sleep-wake rhythm and its clinical significance.

Animal studies provide evidence that the postnatal light environment affects the development of circadian rhythms (Brooks & Canal, 2013). Alternations in natural and artificial photoperiods have also been related to infants' night-time sleep duration (Iwata et al., 2017). Moreover, the development of the sleep—wake rhythm might be related to feeding and social cues (McGraw, Hoffmann, Harker, & Herman, 1999; Mirmiran, Baldwin, & Ariagno, 2003). Finally, although it is clear that environmental factors may affect activity patterns, it has been argued that inter-individual differences in developing circadian rhythms can also be driven by endogenous rhythmicity, possibly more than by the caregivers' influences (Rivkees, 2003). Along these lines, gestational age, birth weight, birth order or breastfeeding duration were not associated with sleep—wake rhythm development (Jenni, Deboer, & Achermann, 2006).

The main aim of the present study was to describe the normative variation in the development of the diurnal sleep-wake rhythm at the ages of 3 and 8 months, and also to assess whether the slower development of the diurnal sleep-wake rhythm is related to sleep

quality, either based on parents' reports or on actigraphy recordings of sleep. Finally, we also evaluated whether the slow development of the diurnal sleep-wake rhythm is related to age, sex, breastfeeding and season of birth.

2 | METHODS

2.1 | Sample

This study is based on the CHILD-SLEEP birth cohort. The sample was recruited during pregnancy in well-baby clinics, approximately at the 32nd week of pregnancy. In total, 1,673 families participated to the study in the study. Specifically for this study, the follow-up time-points were at the ages of 3 and 8 months. Details of the recruitment procedure have been reported elsewhere (Paavonen et al., 2017). The study protocol for the cohort was approved by the local ethical committee (ethical research permission code R11032). The parents gave written informed consent at the beginning of the study.

At 3 months, the response rate was 85.3% (n = 1,427). We excluded infants with severe developmental conditions (such as Down's syndrome or blindness) (n = 11), as reported by the parents by the age of 2 years. A small proportion of the parents (7.1%, n = 101) returned the questionnaires late (age >4 months) and in four cases it was not possible to define the infants' age due to missing data. Therefore, the final sample consisted of 1,311 infants aged 72–120 days (Table 1). As many as 97.0% (n = 1,272) had responded to the Brief Infant Sleep Questionnaire (BISQ); however, 2.4% of them (n = 30) did not have both daytime and night-time sleep durations reported and were thus excluded from further analyses, leaving 1,242 infants aged 3–4 months for the analyses.

At 8 months, the response rate was 77.8% (n=1,302). A few parents (0.5%, n=6) returned the questionnaire late (age >10 months) and in one case it was not possible to define the age of the infant due to missing data. These infants and those with a developmental condition (the same as at the age of 3 months) (n=11) were excluded from the study, leaving 1,284 infants (Table 1). Of these, 99.1% (n=1,272) had responded to the BISQ. Finally, we excluded cases who had missing information on either the daytime or night-time sleep variables (1.1%, n=14), leaving 1,258 infants aged 7–10 months for the analyses.

In addition, a subsample of 372 infants also participated in the actigraph study. Of these, 329 had valid data and were aged 8–10 months at the time of measurement. The cases with severe illnesses (the same as reported above) were excluded from the data, leaving 324 infants for the analyses (155 girls and 174 boys; mean age, 8.1 months; standard deviation [SD], 0.5 months). These infants were randomly selected at birth by contacting the parents in the birth hospital to invite them to the actigraph study. The only exclusion criterion was gestational age <37 weeks. The subsample with actigraph registration did not differ from the main cohort in any of the demographic parameters (all *p*-values >.075).

2.2 | Measures

2.2.1 | Questionnaires

There were separate questionnaires for both parents and their children, filled out by either one parent or both parents together. All three questionnaires comprised several standardized questionnaires and other questions regarding health, welfare and family socioeconomic status. In addition, hospital register data were available for 97.4% (n = 1,278) and 97.7% (n = 1,217) of those eligible at 3 and 8 months, respectively.

To assess infants' sleep duration and sleep quality, we used both the BISQ and the Infant Sleep Questionnaire (ISQ) at 3 and 8 months.

The BISQ is a brief parental questionnaire for screening infant and toddler sleeping problems (Sadeh, 2004). It consists of 13 items, of which we used the following six items: sleep duration during the day (07.00–19.00 hours) and night (19.00–07.00 hours), the number of night awakenings, bedtime, sleep latency and time spent awake at night (22.00–06.00 hours), which are measured as open questions.

The ISQ is a parental questionnaire on sleep quality among infants and toddlers (Morrell, 1999). There are 10 items to study the frequency and severity of difficulties. In this study, we used the following three items: difficulties in settling to sleep (times per week, eight response alternatives), and sleep-onset problems in the evening (minutes in the evening, seven response alternatives) and at night (minutes at night, seven response alternatives). These variables were dichotomized to divide the infants into two groups: those who represent quite typical behaviours for the age and those with sleep difficulties. The cut-off values are reported in Tables 3 and 4.

The development of the diurnal sleep-wake rhythm was evaluated by calculating the percentage of daytime and night-time sleep relative to total sleep duration. Cut-off points for the slow development of a sleep-wake rhythm at 3 and 8 months in this study were set at a proportion of daytime sleep of more than 41.4% and 29.6%, respectively (>75th percentile), based on our own sample.

2.2.2 | Actigraphy

Actiwatch AW7s (manufactured by Cambridge Neurotechnology Ltd) were used in this study. This device uses a validated algorithm (Oakley, 1997) in which activity counts recorded during the measured epoch are modified by the level of activity in the surrounding 2-min time period (i.e., ±2 min) to yield the final activity count for each epoch (Kushida et al., 2001). The parents were asked to place the actigraph around the ankle of their infant for three consecutive days and to carefully keep a sleep log for their infant. Night-time activity data were scored using the Sleep Analysis program provided by the manufacturer and the sleep variables used in this study represent the average values of the measured nights. Bedtimes and wake-up times were defined according to parental reports in the sleep log. The data were thoroughly inspected for any deviances and indicators of mechanical measurement errors. Five registrations were excluded.

2.3 | Statistical analysis

We first studied the distributions of the main variables of interest. Next, using a t test or X^2 test we compared the two groups of infants (those with slower development of a sleep-wake rhythm versus others) relative to background and sleep variables. In order to control for confounding factors (age, gender, breastfeeding and season of birth), we computed multivariate models (analysis of covariance, ANCOVA or logistic regression) to confirm the potential differences in sleep quality between these two groups. In these models, the sleep measures from questionnaires or from actigraphs served as dependent variables, while using the slow development of a sleep-wake rhythm and age, sex, breastfeeding, season of birth and season of actigraph recording as independent variables. The prevalence of sleep-wake rhythm problems was studied using the McNemar test. The infants with persistent problems were defined as those who belonged to the slow development group at both time-points. Finally, we constructed logistic regression models to study factors that are related to slow development. In these models, we used age, sex, breastfeeding and season of birth as explanatory factors. The seasons were defined as the summer solstice season, autumnal equinox season, winter solstice season and spring equinox season, all corresponding to the years of birth and actigraph recordings, respectively.

3 | RESULTS

Differences within sociodemographic variables between infants with and without slow development of their diurnal sleep-wake rhythm at 3 and 8 months are described in Table 1.

As reported in Table 2, at 3 months, the majority of the infants slept less during the day than during the night, with the average percentage of daytime sleep being 36.3%. In addition, this percentage of daytime sleep continued to decrease over the following months, so that at 8 months of age it was 25.6%.

Slow sleep-wake rhythm development was considered to occur in 25.0% (n = 310) of the infants at the age of 3 months and in 25.8% (n = 324) at the age of 8 months.

Overall, 60.1% (n = 654) of the infants did not have developmental sleep-wake rhythm problems at either time-point, whereas 9.7% (n = 105) had them both at 3 and 8 months of age. The distribution was similar at both time-points (p = .826), but there was a tendency for persistent problems (risk ratio, 2.5; 95% confidence interval [CI], 1.9–3.4; negative predictive value, 79.7%; positive predictive value, 39.3%).

As expected, we found that at the age of 3 months, infants with a slow development of the diurnal sleep-wake rhythm were reported to sleep less during the night and more during the daytime. More importantly, they also slept more hours per day, and had a later bedtime, longer sleep-onset latency and more often difficulties settling to sleep; they also spent a longer time awake during the night (see Table 3, Figure 1).

Similarly, at 8 months of age, slow development of a sleepwake rhythm was related to less sleep during the night and more



TABLE 1 Description of the background variables in infants at 3 and 8 months (n = 1,242 at 3 months; n = 1,258 at 8 months)

Three months	Comparison group ($n = 932$)	ison group ($n = 932$) Slow development group ($n = 310$)	
Gender			
Girls, n (%)	423 (45.4%)	164 (52.9%)	.022 ^a
Boys, n (%)	509 (54.6%)	146 (47.1%)	
Age, in days (mean, SD)	96.0 (8.4)	95.6 (8.8)	.484 ^b
Feeding			
Breastfeeding, n (%)	799 (85.9%)	277 (89.6%)	.093ª
Supplemental milk only, n (%)	131 (14.1%)	32 (10.4%)	
Season of birth, n (%)			
Winter (21/12-19/3)	162 (17.4%)	44 (14.2%)	<.001 ^a
Spring (20/3-20/6)	255 (27.4%)	53 (17.1%)	
Summer (21/6-21/9)	323 (34.7%)	109 (35.2%)	
Autumn (22/9-20/12)	192 (20.6%)	104 (33.5%)	
Eight months	Comparison group (n = 934)	Slow development group (n = 324)	p value ^{a,b}
Gender			
Girls, n (%)	446 (47.8%)	151 (46.6%)	.722ª
Boys, n (%)	488 (52.2%)	173 (53.4%)	
Age, in months (mean, SD)	8.2 (0.3)	8.2 (0.3)	.931 ^b
Feeding			
Breastfeeding, n (%)	591 (64.1%)	216 (67.9%)	.217ª
Supplemental milk only, n (%)	331 (35.9%)	102 (32.1%)	
Season of birth, n (%)			
Winter (21/12-19/3)	164 (17.6%)	51 (15.7%)	.149ª
Spring (20/3-20/6)	217 (23.2%)	89 (27.5%)	
Summer (21/6-21/9)	309 (33.1%)	116 (35.8%)	
Autumn (22/9-20/12)	244 (26.1%)	68 (21.0%)	
Season of actigraph, n (%)			
Winter (21/12-19/3)	46 (20.2%)	11 (15.1%)	.682 a
Spring (20/3-20/6)	77 (33.8%)	25 (34.24%)	
Summer (21/6-21/9)	69 (30.3%)	18 (24.7%)	
Autumn (22/9-20/12)	46 (20.2%)	19 (26.0%)	

^aChi-squared test was used in the analysis.

sleep during the daytime. It was also related to longer total sleep per 24 hr, a later bedtime, longer sleep-onset latency, more difficulties settling to sleep and longer time awake during the night (Table 4, Figure 2).

Concerning actigraphy variables, consistent with the questionnaire findings, we found that the infants with slow development of a sleep-wake rhythm spent less time in bed, slept less at night and had later sleep start and end times, than the infants in the comparison group (Table 5). No significant differences were found in sleep latency, actual time awake at night, sleep efficiency, fragmentation index or number of night waking bouts using actigraphy. However, these sleep variables were different between groups using parentreported sleep questionnaires. Using multivariate modelling, we aimed to confirm these results while statistically controlling for potential confounding factors (age, sex, breastfeeding and season of birth). Both at 3 and 8 months, slow development of a sleep–wake rhythm remained significant in all models. Moreover, the sleep variables were variably related to age, sex, breastfeeding and season of birth. For example, at 3 months sleep during the daytime was also explained by younger age (p = .014) and season of birth (p = .028); total sleep by sex (p = .047); and bedtime by sex (p = .049), breastfeeding (p = .001) and season of birth (p = .015). Similarly, at 8 months, daytime sleep was also related to season of birth (p = .008); night-time sleep to age (p = .006) and breastfeeding (p = .047); total sleep to age (p = .001) and season of birth (p = .001); and bedtime to season of birth (p < .001), breastfeeding (p = .017) and sex (p = .036).

^bt test was used in the analysis.

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TABLE 2 Sleep duration and sleep-wake rhythm development at the ages of 3 and 8 months, reported by parents

	Mean	SD	10th percentile	25th percentile	50th percentile	75th percentile	90th percentile
Three months							
Daytime sleep (min)	314	88	210	240	300	360	420
Night-time sleep (min)	546	85	450	498	540	600	630
Total sleep (min)	859	114	720	780	870	930	990
Proportion of daytime sleep (%)	36.3	8.5	25.4	31.0	36.4	41.4	46.2
Proportion of night-time sleep (%)	63.7	8.5	53.8	58.6	63.6	69.0	74.6
Eight months							
Daytime sleep (min)	207	62	135	160	205	240	300
Night-time sleep (min)	593	60	510	555	600	630	660
Total sleep (min)	799	71	720	750	810	840	885
Proportion of daytime sleep (%)	25.6	6.6	17.9	21.2	25.0	29.6	33.7
Proportion of night-time sleep (%)	74.4	6.6	66.3	70.4	75.0	78.8	82.1

TABLE 3 Differences between infants with slow sleep-wake rhythm development and others at 3 months according to questionnaire data

Questionnaire data at	Comparison group, mean (SD)	Slow sleep-wake rhythm development, mean		. 4
3 months	or n (%)	(SD) or n (%)	p values ^{a, b}	p values ^{c,d}
Daytime total sleep (min)	282 (69)	409 (65)	<.001 ^a	<.001 ^c
Night-time total sleep (min)	569 (65)	475 (100)	<.001 ^a	<.001 ^c
Total sleep per 24 hr (min)	851 (99)	883 (147)	<.001 ^a	<.001 ^c
Bedtime (hh:mm)	21:31 (1:03)	22:34 (1:13)	<.001 ^a	.001 ^c
Mean sleep-onset latency (min)	35.6 (30.9)	44.0 (39.8)	.001 ^a	.001 ^c
Difficulties in settling to sleep, n (%)	53 (5.7%)	42 (13.7%)	<.001 ^b	<.001 ^d
Average number of awaken- ings per night	2.2 (1.3)	2.1 (1.2)	.363ª	.118 ^c
Time spent awake during the night (min)	44 (42)	76 (59)	<.001 ^a	<.001 ^c
Long sleep-onset (\geq 30 min) in the evening, n (%)	221 (24.6%)	86 (29.2%)	.122 ^b	.298 ^d
Long sleep-onset (≥20 min) at night, n (%)	144 (16.5%)	62 (22.2%)	.029 ^b	.031 ^d

 $^{^{\}rm a}t$ test, $^{\rm b}X^2$ -test, $^{\rm c}$ ANCOVA, $^{\rm d}$ logistic regression.

Both model types controlled for age, gender, breastfeeding, group and season of birth.

Concerning actigraphy variables, sleep-wake rhythm remained a significant explanatory factor in all multivariate models. In addition, assumed night-time sleep was related to the season in which the actigraphy was recorded (p = .043), while bedtime and sleep ending times were related to season of birth (p-values .035 and .012, respectively), and sleep efficiency was related to sex (p = .023).

Finally, we conducted logistic regression modelling to study the risk factors for the slow development of sleep–wake rhythms at 3 or 8 months. At 3 months, season of birth and sex were related to sleep–wake rhythm development. Girls had a higher risk of problems compared to boys (odds ratio [OR], 1.33; 95% CI, 1.02-1.73; p = .035) and infants born in the summer and autumn had a higher risk of slow

development of sleep–wake rhythms compared to those born in spring (OR, 1.56; 95% CI, 1.08–2.27; p = .018; OR, 2.48; 95% CI, 1.69–3.65). The prevalence rate of slow sleep–wake development was 17.2% in those born in the spring, 25.2% in those born during the summer, 35.1% in those born in the autumn and 21.4% in those born in the winter. At 8 months, no significant risk factors were identified.

4 | DISCUSSION

In this study, we investigated the development of a sleep-wake rhythm in infants of the CHILD-SLEEP birth cohort at 3 and 8 months

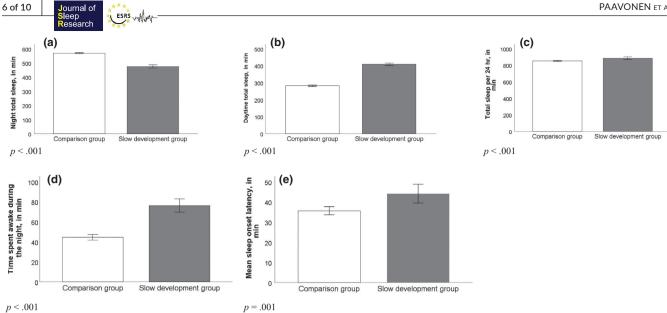


FIGURE 1 Significant differences within sleep quality measured with questionnaires between infants with and without sleep-wake rhythm problems at 3 months of age. These graphs show that infants with sleep-wake rhythm problems at 3 months sleep less at night (a), sleep more during the day (b), have more hours of total sleep per 24 hr (c), spend more time awake during the night (d), and have higher frequency of late sleep onset (>30 min) (e), when compared to infants without sleep-wake rhythm problems. Error bars represent the 95% confidence interval (CI)

TABLE 4 Differences between infants with sleep-wake rhythm problems and others at 8 months according to questionnaire data

Questionnaire data at 8 months	Comparison group, mean (SD) or % (n)	Slow sleep-wake rhythm development, mean (SD) or n (%)	p-values ^{a,b}	p values ^{c,d}
Daytime total sleep (min)	180 (40)	285 (48)	<.001 ^a	<.001 ^c
Night-time total sleep (min)	609 (51)	547 (55)	<.001 ^a	<.001 ^c
Total sleep per 24 hr (min)	788 (66)	832 (75)	<.001 ^a	<.001 ^c
Bedtime (hh:mm)	20:39 (0:47)	21:32 (0:55)	<.001 ^a	<.001 ^c
Mean sleep-onset latency (min)	21.1 (17.3)	25.9 (18.2)	<.001 ^a	<.001 ^c
Difficulties in settling to sleep ≥ 3 times/week (Yes/No)	92 (10.0%)	54 (17.2%)	.001 ^b	.001 ^d
Average number of night awakenings per night	2.4 (1.7)	2.2 (1.5)	.039	.021 ^c
Time spent awake during the night (min)	23 (31)	30 (32)	.001 ^a	.001 ^c
Sleep onset in the evening ≥30 min (Yes/No)	76 (8.4%)	38 (12.3%)	.041 ^b	.057 ^d
Sleep onset at night ≥20 min (Yes/No)	54 (6.2%)	27 (9.3%)	.079 ^b	.194 ^d

^at test, ^bX²-test, ^cANCOVA, ^dlogistic regression.

Both model types controlled for age, gender, breastfeeding, group and season of birth.

of age. We were especially interested in the normative range in the development of sleep-wake rhythms and its clinical significance (i.e., whether slower development is related to sleep quality while confounding factors are controlled).

Previously, only a few longitudinal studies have provided normative reference information on circadian rhythm development and little is known about the individual changes and the stability in infants' sleep-wake behaviour during the first months of life. In this study, 3-month-old infants were found to sleep an average of 5.1 hr

during the daytime, 9.1 hr during the night-time, and 14.1 hr during the whole day, which is in line with previous studies (Bruni et al., 2014; Figueiredo, Dias, Pinto, & Field, 2016). After 3 months of age, the consolidation of sleep towards night-centred sleep occurs and daytime sleep decreases (Bruni et al., 2014; Figueiredo et al., 2016). Consistently, our results showed that 8-month-old infants slept an average of 3.4 hr during the daytime, 9.9 hr during the night-time and 13.3 hr during the whole day.

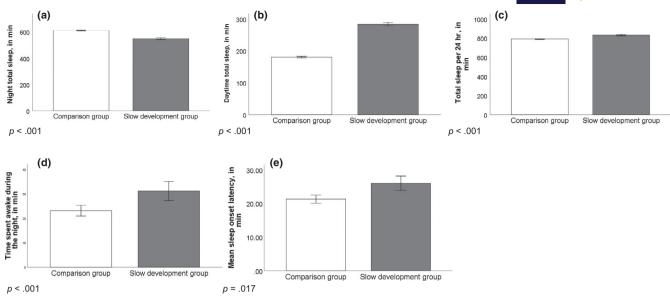


FIGURE 2 Significant differences within sleep quality measured with questionnaires between infants with and without sleep—wake rhythm problems at 8 months of age. These graphs show that infants with sleep—wake rhythm problems at 8 months sleep less at night (a), sleep more during the day (b), have more hours of total sleep per 24 hr (c), have later bedtime (d), spend more time awake during the night (e), and have higher frequency of late sleep onset (> 30 min) (f), when compared to infants without sleep—wake rhythm problems. Error bars represent the 95% confidence interval (CI)

TABLE 5 Differences between infants with slow sleep-wake rhythm development and others according to actigraphy data at 8 months (n = 324)

Actigraph data at 8 months	Comparison group (n = 249), mean (SD)	Slow development group, (n = 75), mean (SD)	p-values ^a	p values ^b
Time in bed (min)	650 (59)	631 (66)	.015	.021
Assumed night sleep time (min)	622 (56)	596 (64)	.001	.001
Actual night sleep time (min)	520 (56)	498 (60)	.004	.003
Night sleep starts (hh:mm)	20:37 (0:49)	21:38 (1:07)	<.001	<.001
Night sleep ends (hh:mm)	7:29 (0:48)	8:09 (1:10)	<.001	<.001
Night sleep latency (min)	17.2 (16.5)	21.4 (17.8)	.068	.121
Actual time awake at night (hh:mm)	1:41 (0:39)	1:37 (0:40)	.490	.647
Night sleep efficiency	79.9 (6.6)	78.6 (6.5)	.174	.126
Fragmentation index	44.8 (10.1)	44.9 (10.5)	.981	.958
Number of night waking bouts	34.7 (9.8)	33.8 (8.3)	.472	.634

^at test, ^bANCOVA.

All models included age, gender, group, season of birth and season of actigraph registration as covariates.

Interestingly, both at 3 and 8 months of age the infants with slower development of sleep-wake rhythm not only slept less during the night and more during the daytime, but they also slept more, had a later sleep-wake rhythm and were more awake during the night, and it took longer for them to fall asleep. These differences remained significant when we controlled for background factors, suggesting that slower diurnal sleep-wake rhythm development is a clinically relevant developmental issue.

Concerning the objective sleep quality measured with the actigraph at 8 months, our questionnaire results were partially supported. The results showed that the infants with slow

development of sleep-wake rhythm spent less time in bed, had fewer hours of assumed and actual sleep during the night, and later sleep onset and waking. However, sleep latency, actual time awake at night and number of night waking bouts, which significantly differed between groups using parent-reported sleep questionnaires, did not show any significant differences between the two groups. These findings are consistent with previous research reporting that objective and subjective sleep measures may be interchangeably used for the assessment of sleep start, sleep end and assumed sleep in children, but not for nocturnal wake times (Werner, Molinari, Guyer, & Jenni, 2008).



Previous studies conducted among toddlers have shown that daytime sleep is relevant in terms of circadian phase and night-time sleep quality. For instance, one study showed that toddlers that habitually napped have later melatonin onset time, later bedtime, longer sleep-onset latency and shorter night-time sleep (Akacem et al., 2015). Another study showed that there was a negative correlation between nap duration, sleep onset time and night-time sleep duration (Nakagawa et al., 2016). These results are in accordance with our findings and suggest that inappropriate amounts of daytime sleep can have a negative effect on subsequent night-time sleep.

We also studied factors that are related to slow diurnal sleepwake rhythm development. Although no significant risk factors were found in 8-month-old infants, the photoperiod during the first 3 months was related to slower development of sleep-wake rhythm at the age of 3 months. This corresponds with findings in animal and infant studies (Brooks & Canal, 2013; Iwata et al., 2017). Exposure to a long photoperiod leads to a phase delay in circadian rhythms and thus also affects the sleep-wake cycle. It should be noted that although the effect of season of birth on sleep-wake cycles might be statistically significant, in young adults and adolescents it affects the preferred sleep onset time rather than the preferred sleep offset time and remains quantitatively small (Natale, Adan, & Fabbri, 2009; Tonetti, Fabbri, Martoni, & Natale, 2011). Furthermore, such an effect was not found in preschool children (Doi, Ishihara, & Uchiyama, 2014), suggesting a major influence of the schedules of society and the circadian preference of the family. However, the development of a sleep-wake rhythm in infants might be more vulnerable to environmental effects of light, particularly in the northern latitudes where the alternations in photoperiods are very large (ranging from 19 hr 35 min in the summertime to 5 hr 25 min in the wintertime in the Tampere area), as suggested by our findings.

Moreover, other factors, such as circadian preference, might also have contributed to these individual differences in sleep functioning. Sleep problems have been found to be greater in evening types compared to morning types, both in toddlers (Simpkin et al., 2014) and preschool children (Jafar et al., 2017), and a change towards the circadian preference for evening hours appears to occur already in toddlers (Randler, Faßl, & Kalb, 2017). In addition, recent findings from our group suggest that maternal circadian preference is related to several sleep difficulties of infants in early childhood, and especially to increased risk of slower sleep-wake rhythm development (Morales-Muñoz et al., 2019).

Although slow development of diurnal rhythm can also represent normative variation, previous research (McGraw et al., 1999; Mirmiran et al., 2003; Rivkees, 2007) suggests that consistent sleep-wake rhythms develop quite rapidly during the first weeks of life, and thus could be moderated by environmental factors (such as differences in parenting or daily activities in these families). If this is confirmed in further studies, these infants might benefit from interventions to support more "age-appropriate" sleep-wake rhythms, which in turn might help them to enhance the quality of their night-time sleep (e.g., less night wakening and

faster sleep onset). In fact, many behavioural interventions include aspects regarding sleep hygiene (i.e., constant bedtime routines) and stable and age-appropriate day-to-night rhythms (Allen, Howlett, Coulombe, & Corkum, 2016). However, intervention studies are needed to gather data on the benefits of sleep-wake rhythm modifications in infants with slower sleep-wake rhythm development.

Taken together, our findings showed that both subjective and objective sleep quality were worse in the infants with slow development of a sleep-wake rhythm, with age, sex, breastfeeding and season of birth as confounding factors. In adulthood and later childhood, circadian rhythm sleep disorders are considered a group of sleep disorders, which affect the timing of sleep, among other aspects of sleep (Dagan, 2002). Our results suggest that already in the early stages of life some common sleeping problems (such as sleep onset problems and night waking) could be connected to delays in diurnal sleep-wake rhythm development.

To date, there is little previous clinical research regarding sleep-wake rhythm development and circadian sleeping problems in infancy. The diagnostic classification systems of sleep disorders do not define specific developmental circadian rhythm problems. According to our findings, slow sleep-wake rhythm development seems to explain some sleeping problems in early childhood (such as sleep onset difficulties and short night-time sleep) and therefore it might be a clinically significant problem, warranting specific attention in clinical settings. It might be possible to improve infant sleep quality by supporting age-appropriate sleep-wake rhythms (by maintaining consistent sleep-wake rhythms and avoiding inappropriately long naps during the daytime). Clinical studies, however, are needed to study the effectiveness of such behavioural interventions.

These findings must be interpreted within the context of potential limitations. First, the criteria for sleep-wake rhythm problems were subjectively determined by parents' report and no objective criteria were used. Second, it is important to notice that in this study we used cut-off values based on our own data, whereas the other study comprising US-Canadian children during the first year of life reported quite different distributions (41% vs. ~35% at the age of 3 months and 30% vs. ~28% at the age of 8 months) (Sadeh et al., 2009). Although there may be cross-cultural differences in sleepwake development, it is also worth noticing that the US-Canadian data were collected via advertising on the internet and therefore might not represent a random sample of infants. More studies on the topic are needed to clarify the normative developmental trajectories in infants. Third, sleep quality was examined with actigraphy at the age of 8 months, but not at 3 months. Therefore, at 3 months we only reported subjective sleep difficulties and thus further studies should aim to include objective data at this age. Fourth, the number of 8-month-old infants who participated in the actigraph study was relatively small compared to the total number of infants in the whole study. In addition, daytime sleep duration was not analysed with actigraphy and thus information about objective total sleep is missing.

To summarize these findings, we found that infant sleep-wake development is highly variable and this variability is related to poorer sleep quality. Thus, some infants may display clinically significant delays in sleep-wake development that may warrant treatment.

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CONFLICT OF INTERESTS

No conflicts of interest declared.

AUTHOR CONTRIBUTIONS

EJP, OSH, AK, PP, TPH and TP designed the study and wrote the protocol. EJP and IMM conducted the statistical analyses and literature reviews. EJP wrote the manuscript. All authors contributed to and approved the final manuscript.

ORCID

E. Juulia Paavonen https://orcid.org/0000-0002-1421-9877

Isabel Morales-Muñoz https://orcid.org/0000-0002-4718-6768

Tiina Paunio https://orcid.org/0000-0002-5560-0666

Anneli Kylliäinen https://orcid.org/0000-0002-8839-3720

Timo Partonen https://orcid.org/0000-0003-1951-2455

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