Sleep Medicine 60 (2019) 13–19

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

Early polysomnographic characteristics associated with neurocognitive development at 36 months of age

Patricia Franco [a, b, *], Aurore Guyon [a, b], Camille Stagnara [c], Sophie Flori [c, d], Flora Bat-Pitault [e], Jian-Sheng Lin [b], Hugues Patural [c, d], Sabine Plancoulaine [f]

[a] Sleep Pediatric Unit, Woman Mother Child Hospital, Hospices Civils de Lyon, Lyon1 University, F-69500, France
[b] Physiology of Brain Arousal System Research Laboratory, CRNL, INSERM-U1028, CNRS UMR5292, Lyon1 University, Lyon, F-69000, France
[c] Neonatal Intensive Care Unit, Department of Pediatric Medicine, CHU de Saint-Etienne, Saint-Etienne, F-42055, France
[d] EA SNA-EPIS Research Laboratory 4607, Jean Monnet University, Saint-Etienne, F-42027, France
[e] Child and Adolescent Psychopathology Unit, Salvator Hospital, Public Assistance-Marseille Hospitals, Aix-Marseille II University, Marseille, F-13000, France
[f] INSERM, UMR1153, Center for Research in Epidemiology and StatisticS (CRESS), EArly life Research on later Health Team (EARoH), Univ Paris-Descartes, Paris, France

ARTICLE INFO

Article history:
Received 12 July 2018
Received in revised form
13 November 2018
Accepted 17 November 2018
Available online 5 January 2019

Keywords:
Sleep
Intelligence quotient
Preschoolers
Cohort study
Arousal
Infant

ABSTRACT

Background: Few studies on the relationship between sleep quantity and/or quality and cognition have been conducted among preschoolers from the healthy general population. We aimed to identify, among 3-year-old children, early polysomnography (PSG) sleep factors associated with estimated intelligence quotient (IQ) using the Weschler Preschool and Primary Scale Intelligence-III test (WPPSI-III) and its indicators: full-scale (FISQ), verbal (VIQ), and performance (PIQ) intelligence quotients.
Methods: We included full-term children from the French birth-cohort AuBE with PSG recording at term (M0) and/or six months (M6), and available WPPSI-III scores at three years. Sleep and arousal characteristics of these infants were evaluated during day and night sleep periods. Relationships between IQ scores and sleep parameters were estimated using models with the child as a repeated effect adjusted for time (night/day), maturation (M0/M6), tobacco exposure (yes/no), anxiety-depressive scores during pregnancy, maternal age, duration of breastfeeding and child's gender.
Results: A total of 118 PSG recordings were obtained, representing a total of 78 unique children (38 with one PSG and 40 with two PSG). No correlations were found between night and day sleep durations at M0 or M6. Mean VIQ, PIQ, and FSIQ scores were within normal ranges. In multivariate models, longer sleep duration and higher sleep efficiency during the day were negatively associated with all IQ scores. More frequent arousals during the night were associated with lower VIQ scores.
Conclusion: Early sleep characteristics such as night sleep fragmentation or longer naps could be associated with impaired cognitive function at three years of age.

1. Introduction

Sleep is a dynamic developmental process, particularly in the first year of life. Multiple studies have found relationships between sleep and cognitive benefits in school-aged children [1–4]; however, there have been fewer studies regarding the effects of infants' sleep on cognitive outcomes [5].

Two cross-sectional studies that included typically developing infants were used to evaluate this relationship via questionnaires, sleep logs, and actigraphic recordings [6,7]. The authors reported that greater sleep efficiency measured via sleep actigraphic data was positively correlated with mental development in 10–13 month-old infants [6,7] and that greater number of movements or activity during sleep and a greater number of awakenings after sleep onset were negatively correlated with cognitive function [6]; in both studies there were no significant associations between parental sleep reports and any of the cognitive measures.

Longitudinal studies conducted by Bernier et al. found that a higher proportion of night sleep (with regard to total sleep) at 12–13

Abbreviations: AS, Active Sleep; BMI, Body Mass Index; FSIQ, Full-Scale intelligence quotient; HAD, Hospital Anxiety and Depression scale; IQ, intelligence quotient; PIQ, performance intelligence quotient; PSG, polysomnography recording; QS, Quiet Sleep; SD, Standard Deviation; VIQ, verbal intelligence quotient; WPPSI-III, Weschler Preschool and Primary Scale Intelligence test.

* Corresponding author. Hôpital Femme Mère Enfant, 59, boulevard Pinel, 69500 Lyon, France. Fax: +33427 869 230.
E-mail address: Patricia.Franco@univ-lyon1.fr (P. Franco).

https://doi.org/10.1016/j.sleep.2018.11.026
1389-9457/

and 18 months of age predicted better executive functioning at 18, 26, and 48 months of age [8,9]; these studies found no relationship between sleep duration at 12 months of age and general cognitive functioning at 48 months [8]. These results were independent of confounders such as socioeconomic status. Contrary to the latter studies, Sheridan et al. reported that the relationship observed between sleep disturbance at 12 and 18 months and lower intelligence quotient (IQ) scores at five years of age, was no longer statistically significant after adjusting for psychosocial adversity [10]. Recently, we evaluated the relationship between sleep data collected via questionnaires at birth, six, 12, 18, and 24 months and the Weschler Preschool and Primary Scale Intelligence-III (WPPSI-III) scores at three years of age in 194 children from the French birth-cohort AuBE [11]. We found that night awakenings at six months of age and frequent snoring at 18 months of age were negatively associated with performance IQ (PIQ) at three years of age. We also found a positive association between day/night sleep ratio at 12 months and PIQ. Conversely, in a longitudinal study that included 1029 twins, Dionne et al. found that day/night sleep ratios at six and 18 months of age were negatively associated with language skills at five years of age [12]. However, the sleep data in all of these longitudinal studies were only obtained from parental reports.

The objective of the present study was to identify, in 3-year-old children from the French birth-cohort AuBE, macro- and microstructure sleep characteristics during day and night at term (M0) and at six months of age (M6) associated with IQ estimated through WPPSI-III and its indicators: full-scale (FSIQ), verbal (VIQ) and performance (PIQ) and their sub-scale scores such as the general language composite score (GLC). Confounders such as the child's age in days and period at PSG recording (M0)/M6), maternal age at delivery, tobacco consumption during pregnancy, depressive anxiety score on the questionnaire during pregnancy, socioeconomic level, child gender, and duration of breastfeeding were also taken into account.

2. Methods

2.1. Study design and questionnaires

The Autonomic Baby Evaluation (AuBE) study was a prospective study to assess the relationship between autonomic and sleep maturation on psychometric development in a cohort of term and preterm newborns at three years of age. The study design has previously been published [13]. The AuBE study was conducted at the University Hospital of Saint-Etienne (France), a level III university maternity ward with neonatal intensive care units and 3500 births annually. Infants were included in the study over the 24 months from September 2009 to September 2011. Only healthy infants who were born with a term $\geq$37 weeks gestational age were included in this study (N = 299). Pregnancy data were collected from mothers following births (parity, maternal age at delivery, maternal tobacco consumption or nicotine substitutes during pregnancy, as well as the assessment of anxiety and depression trends by the Hospital Anxiety Depression (HAD) self-administered questionnaire. The socioeconomic level of the mothers was coded as follows: 0 (no qualifications, unemployed, or manual), 1 (employed, manager). Child gender, gestational age, birth weight, and duration of breastfeeding (never, $\leq$3 months, >3 months) were also collected.

2.2. Polysomnograms

24h-polysomnograms were performed following birth (usually the second day; M0) in the maternity unit and at six months (M6) at home and analyzed as previously described [14]. Briefly, the polysomnograph (Dream®, Medatec, Bruxelles, Belgium) simultaneously recorded frontal, central and occipital leads (FP2, C4, O2, A1), two electrooculograms, 1 chin electromyogram and 1 electrocardiogram, chest and abdominal respiratory movements by inductance plethysmography, as well as noninvasive arterial oxygen saturation using an oximetry probe placed on the foot. Polysomnograms of newborn children were analyzed at 30-second intervals and classified as Quiet Sleep (QS), Active Sleep (AS), or Indeterminate Sleep (IS) according to Guilleminault and Souquet criteria [15]. Since we wanted to evaluate sleep maturation from birth to six months of age, we used the same criteria to score sleep stages at six months: QS for Non-Rapid Eye Movement (NREM) Sleep and AS for Rapid Eye Movement (REM) sleep. Sleep stages were expressed as a percentage of total sleep time. Time awake represented the proportion of total recording time. Sleep efficiency was defined by dividing total sleep time by total recording time, multiplied by 100. Arousability is not a state, but a continuous process from subcortical to cortical areas; cortical arousal or microarousal (MA) was scored if there was an abrupt change in EEG background frequency of at least 1 Hz for a minimum of three seconds, while at least two of the following changes occurred at the same time: 1) a large body movement detected by movement sensors or seen as an artifact movement in the somatic channels (ECG, EEG, respiratory parameters), 2) changes in heart rate of at least 10% of baseline values; 3) changes in breathing pattern, frequency and/or amplitude, in QS, or increase in chin EMG tonus in AS [16]. The frequencies of arousal events were measured by dividing the total number of episodes by the total sleep time in minutes and multiplying by 60. Baseline sleep states that preceded arousals were established during 30-second intervals. At least 10 seconds of an uninterrupted state was required between arousals. Awakening was defined as cortical arousal, as defined above, lasting 1 minute or more and meeting the Anders, Emde and Parmelee criteria for wakefulness [17]. We compared the sleep and arousal results between 8:00 PM to 8:00 AM (night) and 8:00 AM to 8:00 PM (day).

2.3. Psychometric assessment

One psychologist administered the WPPSI-III test to all children followed to 36 months of age (N = 195) avoiding test administrator variability. Children were evaluated using the five subtests as recommended for their age group (30–47 months): Receptive Vocabulary, Block Design, Information, Object Assembly, and Picture Naming. The WPPSI-III provides subtest and composite scores that represent intellectual functioning in verbal and performance cognitive domains (named VIQ and PIQ, respectively), and a composite score that represents the child's general intellectual ability (ie, Full-Scale IQ or FSIQ). Also, an ancillary index score was calculated: the general language composite score (GLC).

2.4. Ethics

The local research ethics committee approved the study. Written informed consent was obtained at enrolment from the parents. The study was registered in the International Clinical Trials Registry (ClinicalTrials.gov, ID NCT00951860).

2.5. Statistical analyses

Only infants who had at least one available PSG recording at M0 or M6 and a WPPSI test at age three years of age were included in the current study. Descriptive analyses were performed using Chi-square and *t*-tests. Fisher's exact test was used when needed. Pearson correlations were estimated between sleep characteristics.

Multivariate analyses were performed to estimate relationships between IQ scores and sleep characteristics. Thus, the response variables were the variables of interest, ie, the IQ scores (VIQ, PIQ, FISQ, GLC). The explicative variables were time (night/day), maturation (M0/M6), tobacco exposure (yes/no), HAD, maternal age, breastfeeding duration, child gender. Models were performed considering in addition as explicative variable one sleep parameter at a time (Total Sleep Time - TST, Sleep Efficiency - ES, AS%, QS%, Arousals/h, Arousals in AS/h and in QS/h) and including two or more of them when correlations between sleep characteristics were observed. Generalized linear models were constructed, with the child as a repeated effect. Statistical significance was defined with a level of $p < 0.05$. All analyses were performed using SAS software (version 9.4, SAS Institute, Cary, NC, USA).

3. Results

3.1. Population characteristics

A total of 118 PSG recordings were included in the current study representing a total of 78 different children (38 children with one PSG recording and 40 with two PSG recordings).

Included children (N = 78) compared to the initial AuBE sample (N = 221) were breastfed for a longer period (36% vs. 21% were breastfed for more than three months, p = 0.02), had a longer gestational age (mean ± SD: 40 ± 1 vs. 39 ± 3 weeks, p = 0.0005), had lower mean FSIQ (95 ± 13 vs. 102 ± 12, p = 0.0007), VIQ (103 ± 16 vs. 108 ± 13, p = 0.01), PIQ (89 ± 10 vs. 94 ± 13, p = 0.0009) but similar GLC (104 ± 15 vs. 108 ± 13, p = 0.06). No difference in gender, maternal age, maternal parity, maternal professional activity, maternal anxiety or depressive evaluation (HAD scores) were observed. Characteristics of the included population are presented in Table 1.

3.2. Sleep characteristics

Table 2 presents the PSG characteristics according to the time of recording. There was no significant correlation between night and day sleep durations at M0 or M6 (p > 0.25). As previously published [14], compared to day sleep, night sleep was significantly longer and more efficient at both M0, but especially at M6, at which time there was also a significantly greater proportion of quiet sleep (QS) and a significantly smaller proportion of active sleep (AS). There were also significantly more arousals in AS during day sleep at M0 and during night sleep at M6. Table 3 presents correlations between the main sleep characteristics. At M0, night sleep duration was significantly correlated with night and day sleep efficiency and inversely correlated with night and day arousals (MA). Night sleep efficiency (SE) was inversely correlated with night and day MA. Day sleep duration had the same effects on SE and MA but only on day sleep periods. There was a positive correlation between MA during night and day sleep. At M6, the effects were less marked with a positive correlation between sleep duration and sleep efficiency in both night and day sleep periods.

Table 1
Maternal and children' characteristics.

	% (N) or Mean (±SD)
Maternal characteristics	
Socioeconomic level	
unemployed/manual worker	24.4 (19)
employed/manager	75.6 (59)
Age at delivery (years)	31 (±4)
Parity	
1st child	38.5 (30)
2nd child	37.1 (29)
≥3rd child	24.4 (19)
Tobacco consumption during pregnancy	30.8 (24)
Depressive score (HAD≥8)	5.1 (4)
Anxiety score (HAD≥8)	35.9 (28)
Child characteristics	
Gender (Girls)	47.4 (37)
Gestational age (WA)	39.7 (±1)
Birth weight (g)	3263 (±388)
Breastfeeding duration	
Never	33.3 (26)
≤3 months	30.8 (24)
>3 months	35.9 (28)
IQ scores	
FSIQ	95 (±13)
PIQ	89 (±10)
VIQ	103 (±16)
GLC	104 (±15)

3.3. Multivariate analysis

Longer day sleep duration was negatively associated with FSIQ score at 36 months, especially in verbal performances (VIQ and GLC); higher SE during day sleep was associated with a lower score for all IQ scales. More frequent MA during the night was associated with lower VIQ and GLC scores. However, more frequent MA during the day was associated with higher verbal scores (VIQ and GLC scores) and with a tendency to higher FISQ (Table 4). When TST and SE were included together (with or without MA), associations between day sleep duration, day SE and FSIQ were no longer significant suggesting that they predict the same phenomenon while the other initially observed associations remained (data is not shown/supplemental table) suggesting independent predictions.

4. Discussion

4.1. Night sleep fragmentation and neurocognitive development at 36 months

We report for the first time an association between night sleep fragmentation, objectively measured by polysomnography in the early months of life and lower verbal performance scores at 36 months of age. These results are in agreement with other studies that used objective sleep evaluation such as actigraphy [6,7], but also with a previous study that we reported which used parental night awakening reports at six months [11]. Other authors report that fragmented sleep has been associated with memory difficulties and poorer academic achievement in older children [18] probably due to lower sleep efficiency throughout childhood [19].

Numerous mechanisms could be implicated in the relationship between sleep quality and cognitive function.

Sleep is described as a powerful aid in memory consolidation [20]; in adults performances obtained during cued-recall of verbal (word-pairs) or visuospatial (a pair of cards) material are better after post-learning sleep than after a similar period spent awake [21–23]. A preserved sleep organization, characterized by uninterrupted cycles of slow wave sleep (SWS) and paradoxical sleep (PS), seems to be a necessary framework for effective sleep-dependent memory consolidation processes [24]. The experimental disturbance of sleep architecture [25] or the disorganization of sleep cycles observed in the elderly [26,27] are detrimental to verbal memory consolidation. During the cyclic succession of SWS and PS periods, a complex dialogue between the hippocampus and the neocortex leads to memory trace consolidation [28].

As observed in adults, sleep also has a beneficial effect on the consolidation of several episodic memories in infants [29] and

Table 2
Polysomnographic data: night and day sleep characteristics of the infants at M0 and M6.

Mean (SD)	M0			M6		
	NIGHT	DAY	p-value	NIGHT	DAY	p-value
TST (Min)	417 (116)	248 (79)	<10−4	534 (128)	94 (63)	<10−4
SE (%)	57.7 (14.7)	51.5 (16.2)	0.01	83.4 (13)	23.5 (14)	<10−4
QS%	49.8 (16.6)	48.8 (15.7)	0.16	57.9 (9.5)	67.3 (26.3)	0.003
AS%	49.2 (15.8)	46.3 (18.9)	0.84	41.6 (9.3)	28.2 (23.6)	0.03
MA (/h)	20 (8.1)	33 (19.9)	<10−4	14.9 (6.0)	12.8 (8.4)	0.34
MA−AS (/h)	30.4 (14.1)	36.1 (14.4)	0.06	25.1 (9.7)	17.7 (13.4)	0.003
MA-QS* (/h)	10.7 (0−49)	12.2 (0−66)	0.30	6.7 (0.5−35.7)	4.5 (0−51.4)	0.02

M0: term; M6: 6 months; TST: total sleep time; SE: sleep efficiency; AS%: active sleep; QS%: quiet sleep; MA: micro-arousals; MA−AS: micro-arousals in Active Sleep; MA-QS: micro-arousals in Quiet Sleep.
* MA-QS had non-Gaussian distribution and was summarized by median and range (minimum−maximum).

children [23,30,31]. Contrary to adults, no sleep consolidation effect has been found for procedural memory in children [23,32]. Thus, when sleep is fragmented or disturbed, sleep-dependent memory consolidation processes are also disturbed in children, as shown in children with attention-deficit/hyperactivity disorder [31] or with sleep-disordered breathing (SDB) [32]. Children with SDB exhibited lower performances than control children during both learning and recall sessions of a story recall test [32], greater attention deficit, reduced IQ scores, and lower school performance [33]. Unfortunately, due to the AuBe study schedule, we did not have thermistors or nasal cannulae to evaluate the presence of obstructive breathing potentially responsible for respiratory-related arousals. Indeed, using over-night PSG in 8-month old infants, Montgomery−Downs et al. showed that snore-related arousals, in the absence of apneas or hypopneas, are negatively correlated with mental scores [34]. In the previous study that we reported, frequent snoring observed by parents at 18 months was associated with lower PIQ and Block Design scores at three years of age [11].

However, the exact mechanisms relating sleep and cognition remain to be understood and in particular, why early sleep characteristics could impact cognitive development during childhood. For some authors, it is suggested that low sleep quality during infancy may predict low sleep efficiency during childhood, and thus low cognitive function [35]. Moreover, cognitive acquisitions could be significantly impeded by chronically altered sleep duration or sleep quality throughout childhood. Another possibility would be that there is a critical period in early childhood in which the lack of sleep quality or quantity could be particularly detrimental to various aspects of brain development, even if sleep duration normalizes later on [35]. This latter hypothesis, studied in preterm children and children with obstructive sleep apnea syndrome [36], is in accord with the Barker hypothesis, now called the Developmental Origins of Health and Disease (DOHaD) that linked several exposures during development (as nutrition, stress or chemicals) to latter heath troubles [37].

4.2. Sleep duration/quality during the day and neurocognitive development at 36 months

In the present study, we found that longer sleep duration and higher sleep efficiency during daytime were negatively associated with all IQ scales. There are, however, controversial results asserting the benefits of napping for learning and memory, especially in younger children [38].

Some authors suggest an important role for daytime sleep to consolidate memory performance during the first years of life.

Gomez and al. showed that 15-month-old infants who napped were able to abstract the general grammatical pattern of a briefly presented artificial language [39] and to remember the general grammatical pattern 24h later, while those who did not nap showed no evidence of remembering anything [40]. More recently Giganti et al. reported that a nap benefits explicit memory consolidation among children aged three to six years but not in implicit perceptual learning (naming pictures) [41]. Kurdziel et al. reported that naps help in memorization and learning especially regarding visuospatial tasks (Memory game) among preschoolers aged between 36 and 67 months; they also reported that long-term benefits on memory consolidation was greatest for children who napped habitually [42]. Even more, when considering naturally occurring sleep, Lukowski et al. showed that daytime nap duration was positively associated with immediate imitation encoding, in particular, encoding in a correct temporal order, as well as with delayed recall in the generalization of temporal order information, in 10-month-old infants, while night-time sleep duration was not associated with immediate or delayed recalls [43].

On the contrary, for other authors, daytime sleep could be a negative factor for cognitive function.

The progressive disappearance of a nap in favor of night sleep (called sleep consolidation) may be seen as a global marker of brain maturity [6,7]. Bernier et al. showed among 65 children that an increase % of sleep during the night in relation to the day

Table 3
Correlations between sleep characteristics.

		M0						M6					
		TST		SE		MA		TST		SE		MA	
		Night	Day	Night	Day	Night	Day	Night	Day	Night	Day	Night	Day
TST	Night	1.00	0.13	0.89***	0.35***	−0.71***	−0.66***	1.00	0.10	0.57***	0.22	0.12	0.07
	Day		1.00	0.05	0.65***	−0.02	−0.08		1.00	0.10	0.79***	−0.05	0.25
SE	Night			1.00	0.18	−0.65***	−0.66***			1.00	0.08	0.04	0.15
	Day				1.00	−0.26	−0.27*				1.00	0.16	0.29
MA	Night					1.00	0.83***					1.00	0.24
	Day						1.00						1.00

*p < 0.05, **p < 0.01, ***p < 0.001.
M0: term; M6: 6 months; TST: total sleep time; SE: sleep efficiency; MA: micro-arousals.

Table 4
Multivariate models coefficients and p-values with IQ scores as response and each night- and day-sleep characteristic (TST, SE, AS%, QS%, MA, MA–AS or MA-QS) as explicative variables. Each model additionally accounted for the child's age in days and period at EEG recording (M0/M6) and was adjusted on maternal age at delivery, tobacco consumption during pregnancy, anxiety score on HAD questionnaire during pregnancy, socioeconomic level, child's gender, gestational age, and breastfeeding duration.

	FISQ		PIQ		VIQ		GLC	
	Beta (95%CI)	p-value	Beta (95%CI)	p-value	Beta (95%CI)	p-value	Beta (95%CI)	p-value
TST								
Night	0.006 (−0.01; 0.02)	0.49	0.003 (−0.01; 0.02)	0.64	0.006 (−0.02; 0.03)	0.57	0.005 (−0.02; 0.03)	0.66
Day	−0.03 (-0.05; -0.001)	0.05	−0.01 (−0.03; 0.01)	0.36	−0.04 (-0.07; -0.003)	0.03	−0.04 (-0.07; -0.01)	0.01
SE								
Night	0.08 (−0.08; 0.24)	0.33	0.05 (−0.06; 0.16)	0.39	0.07 (−0.14; 0.29)	0.49	0.08 (−0.14; 0.29)	0.49
Day	−0.14 (-0.26; -0.02)	0.02	−0.13 (-0.22; -0.04)	0.005	−0.12 (−0.29; 0.04)	0.13	−0.20 (-0.35; -0.05)	0.01
AS%								
Night	−0.14 (−0.36; 0.08)	0.21	−0.03 (−0.19; 0.13)	0.72	−0.19 (−0.45; 0.06)	0.14	−0.19 (−0.46; 0.08)	0.17
Day	0.06 (−0.09; 0.21)	0.44	−0.009 (−0.13; 0.11)	0.88	0.09 (−0.09; 0.273)	0.31	0.04 (−0.15; 0.23)	0.66
QS%								
Night	0.06 (−0.13; 0.24)	0.55	−0.02 (−0.16; 0.13)	0.81	0.11 (−0.12; 0.33)	0.36	0.11 (−0.13; 0.35)	0.36
Day	0.02 (−0.08; 0.12)	0.69	0.06 (−0.03; 0.15)	0.21	−0.008 (−0.13; 0.12)	0.91	0.02 (−0.12; 0.16)	0.76
MA								
Night	−0.39 (−0.80; 0.02)	0.06	−0.16 (−0.54; 0.22)	0.42	−0.49 (-0.93; -0.05)	0.03	−0.60 (-1.05; -0.15)	0.01
Day	0.18 (-0.003; 0.37)	0.05	0.07 (−0.10; 0.24)	0.43	0.24 (0.03; 0.44)	0.02	0.27 (0.03; 0.51)	0.03
MA–AS								
Night	−0.09 (−0.30; 0.12)	0.39	−0.07 (−0.27; 0.12)	0.45	−0.08 (−0.33; 0.17)	0.52	−0.13 (−0.38; 0.12)	0.30
Day	0.05 (−0.12; 0.23)	0.57	0.04 (−0.14; 0.23)	0.64	0.04 (−0.14; 0.23)	0.65	0.08 (−0.15; 0.31)	0.48
MA-QS								
Night	0.57 (−1.13; 2.26)	0.51	0.23 (−1.20; 1.67)	0.75	0.95 (−1.19; 3.09)	0.38	1.22 (−0.92; 3.35)	0.26
Day	−0.34 (−1.66; 0.98)	0.61	−0.22 (−1.54; 1.09)	0.74	−0.62 (−2.13; 0.89)	0.42	−0.95 (−2.59; 0.68)	0.25

TST: total sleep time; SE: sleep efficiency; AS%: active sleep; QS%: quiet sleep; MA: micro-arousals; MA–AS: micro-arousals in Active Sleep; MA-QS: micro-arousals in Quiet Sleep. MA-QS had non-Gaussian distribution and was log base 2 transformed.

at 12 months of age was associated with better executive functioning (Matrix Reasoning subscale from the WPSSI III) at four years of age, taking into account previous socioeconomic status and prior cognitive functioning measured at one and two years of age [8]. Also, Dione et al. showed, among 1029 twins, that more daytime in relation to night sleep at six and 18 months of age was negatively associated with language skills at 30 and 60 months of age [12].

Excessively long nap durations may also interfere with children's exploration of their physical and social environment and thereby possibly impede their optimal development [44].

However, the most consistent finding in the literature was a negative association between day and night sleep. More daytime sleep is associated with later onset, shorter duration and poorer quality of night sleep, with the strongest evidence after the age of two years [38]. However, in the present study, we did not find a correlation between night and day sleep duration.

Discrepancies between the positive and negative effects of a nap on cognition could be explained by the differences in the performed tests but also by the variables considered for adjustment. In our study, all cognitive functions were impaired. Day sleep duration specifically affected the verbal quotient, although day sleep efficiency influenced the performance quotient. Another important factor could be the changing value of napping over time. The present study refers to the first six months of life, as in the study reported by Dione et al. [12]; at this age, naps have more AS and less QS than later in the life.

Most studies reported the effects of nap duration on cognitive function and development. How could we explain the negative effect of early nap sleep efficiency on cognition?

As noted, we found a positive association between day sleep quality (high sleep efficiency and fewer arousals) and lower VIQ and FSIQ. The first possibility is sleep duration. In both night and day sleep, we found a positive correlation between sleep duration and sleep efficiency. Better sleep quality is related to longer sleep duration. Our results showed that when TST and SE predict the same outcome they represent the same phenomenon, they are not independent; however, arousals, whatever the model, is an independent predictor of IQs. Arousal processes do not always proceed to completion (a full awakening) [45,46], and thus do not represent the same measure as awakenings and sleep efficiency.

As a reflection of the general nature of arousability, we found a positive correlation between the frequency of arousals during the night and during the day. Frequent arousals could have a deleterious effect on night sleep efficiency. Indeed, we showed that higher sleep efficiency during the night was negatively correlated with arousals during the night and the day. These results were only found at term (M0) and not at six months (M6). As shown in our previous work, maturation of spontaneous arousals from sleep differed between day and night sleep [14]. With age, arousals especially during AS/REM increased during night sleep but decreased during the day. Further studies should be conducted to better understand the underlying mechanisms of arousals and their maturation.

4.3. Limitations

First, the present study included a small number of subjects. This may lead to a lack of power to detect an effect (ie, the effect of night sleep duration [44,47], sleep stages [35], gender.). From the first months of life, girls sleep longer than boys [48] and therefore impairments in sleep duration and quality could have different effects according to gender [49]. Second, we did not have a thermistor or nasal cannula to detect sleep-disordered breathing; we did not use more sophisticated markers of sleep fragmentation such as Cycling Alternating Patterns [50]. Third, due to our recruitment method, based on voluntary participation in the study, and to the attrition during follow-up, there is an over-representation of middle–high working class mothers, compared to the national population [51], limiting the generalization of the results. Fourth, these were secondary analyses, and only partial information was available regarding some potential risk factors. For example, no information on parental origins or ethnic group was collected, and no information on maternal IQ or educational level

were available; these were approximated via work category. Finally, the maturation of central nervous system structures such as the hypothalamus or the neurotransmitter system underlies both cognitive development and the regulation of sleep/wake cycles [50]. However, the exact mechanisms relating sleep and cognition remain to be understood.

5. Conclusion

For the first time with objective sleep data obtained by polysomnography recordings in infancy, we found that sleep characteristics such as night sleep fragmentation or day sleep duration/quality could be associated with impaired cognitive function at three years of age. Further studies are needed to confirm these results in larger samples of children from the general healthy population and to examine whether these modifications track throughout childhood. This is important to understand because sleep is one early life factor that can be targeted for intervention to optimize early development.

Specific funding

None.

Acknowledgments

The AuBE study is allowed through consecutive grants from the French Ministry of Health: *Programmes Hospitaliers de Recherche Clinique* – PHRC interregional, 2009 and AOL 2010. The neuropsychological evaluation and the study were made possible through grants from laboratories Abbott-France, Nestlé-France and the association ADERPS (Saint-Etienne non-profit organization for the pediatric research development – University Hospital of Saint-Etienne – France).

We especially acknowledge Mrs. Sophie Foucat and all the parents of the association SA VIE (www.sa-vie.fr; Nantes-France), Dr. Elisabeth Briand-Huchet and Mrs. Myriam Morinay, president of the French national non-profit organization NAITRE et VIVRE (naitre-et-vivre.org) for supporting the development and funding of research on Sudden Infant Death Syndrome.

We finally thank the parents and children of the AuBE cohort without whom this great adventure could not go on.

Conflict of interest

None in relation with this article.

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.sleep.2018.11.026.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sleep.2018.11.026.

References

[1] Gruber R, Laviolette R, Deluca P, et al. Short sleep duration is associated with poor performance on IQ measures in healthy school-age children. Sleep Med 2010;11:289–94.
[2] Sadeh A, Gruber R, Raviv A. The effects of sleep restriction and extension on school-age children: what a difference an hour makes. Child Dev 2003;74:444–55.
[3] Paavonen EJ, Raikkonen K, Pesonen AK, et al. Sleep quality and cognitive performance in 8-year-old children. Sleep Med 2010;11:386–92.
[4] Touchette E, Petit D, Seguin JR, et al. Associations between sleep duration patterns and behavioral/cognitive functioning at school entry. Sleep 2007;30:1213–9.
[5] Tham EK, Schneider N, Broekman BF. Infant sleep and its relation with cognition and growth: a narrative review. Nat Sci Sleep 2017;9:135–49.
[6] Scher A. Infant sleep at 10 months of age as a window to cognitive development. Early Hum Dev 2005;81:289–92.
[7] Gibson D, Elder D, Gander P. Actigraphic sleep and developmental progress of one-year-old infants. Sleep Biol Rhythm 2012;10:77–83.
[8] Bernier A, Beauchamp MH, Bouvette-Turcot AA, et al. Sleep and cognition in preschool years: specific links to executive functioning. Child Dev 2013;84:1542–53.
[9] Bernier A, Carlson SM, Bordeleau S, et al. Relations between physiological and cognitive regulatory systems: infant sleep regulation and subsequent executive functioning. Child Dev 2010;81:1739–52.
[10] Sheridan A, Murray L, Cooper PJ, et al. A longitudinal study of child sleep in high and low risk families: relationship to early maternal settling strategies and child psychological functioning. Sleep Med 2013;14:266–73.
[11] Plancoulaine S, Stagnara C, Flori S, et al. Early features associated with the neurocognitive development at 36 months of age: the AuBE study. Sleep Med 2017;30:222–8.
[12] Dionne G, Touchette E, Forget-Dubois N, et al. Associations between sleep-wake consolidation and language development in early childhood: a longitudinal twin study. Sleep 2011;34:987–95.
[13] Patural H, Pichot V, Franco P, et al. Autonomic nervous system: a biomarker of neurodevelopmental comportment-the AuBE study. J Clin Trials 2014;4:176–83.
[14] Gillioen B, Plancoulaine S, Montemitro E, et al. Maturation of arousals during day and night in infants with non-smoking and smoking mothers. Early Hum Dev 2017;115:46–50.
[15] Guilleminault C, Souquet M. Sleep states and related pathology. In: Korobkin R, Guilleminault C, editors. Advances in perinatal Neurology; 1979. p. 225–47.
[16] Arousals IPWGo. The scoring in healthy term infants (between the ages of 1 and 6 months). J Sleep Res 2005;14:37–41.
[17] Anders T, Emde R, Parmelee A. A manual of standardized terminology, techniques and criteria for scoring of states of sleep and wakefulness in newborn infants. Los Angeles: UCLA Brain Information Service/BRI Publications Office; 1984.
[18] O'Brien LM. The neurocognitive effects of sleep disruption in children and adolescents. Child Adolesc Psychiatr Clin N Am 2009;18:813–23.
[19] Tikotzky L, Shaashua L. Infant sleep and early parental sleep-related cognitions predict sleep in pre-school children. Sleep Med 2012;13:185–92.
[20] Diekelmann S, Wilhelm I, Born J. The whats and whens of sleep-dependent memory consolidation. Sleep Med Rev 2009;13:309–21.
[21] Gais S, Born J. Declarative memory consolidation: mechanisms acting during human sleep. Learn Mem 2004;11:679–85.
[22] Gais S, Lucas B, Born J. Sleep after learning aids memory recall. Learn Mem 2006;13:259–62.
[23] Wilhelm I, Diekelmann S, Born J. Sleep in children improves memory performance on declarative but not procedural tasks. Learn Mem 2008;15:373–7.
[24] Ambrosini MV, Giuditta A. Learning and sleep: the sequential hypothesis. Sleep Med Rev 2001;5:477–90.
[25] Ficca G, Lombardo P, Rossi L, et al. Morning recall of verbal material depends on prior sleep organization. Behav Brain Res 2000;112:159–63.
[26] Mazzoni G, Gori S, Formicola G, et al. Word recall correlates with sleep cycles in elderly subjects. J Sleep Res 1999;8:185–8.
[27] Cherdieu M, Reynaud E, Uhlrich J, et al. Does age worsen sleep-dependent memory consolidation? J Sleep Res 2014;23:53–60.
[28] Born J, Wilhelm I. System consolidation of memory during sleep. Psychol Res 2012;76:192–203.
[29] Seehagen S, Konrad C, Herbert JS, et al. Timely sleep facilitates declarative memory consolidation in infants. Proc Natl Acad Sci U S A 2015;112:1625–9.
[30] Backhaus J, Hoeckesfeld R, Born J, et al. Immediate as well as delayed post learning sleep but not wakefulness enhances declarative memory consolidation in children. Neurobiol Learn Mem 2008;89:76–80.
[31] Prehn-Kristensen A, Goder R, Fischer J, et al. Reduced sleep-associated consolidation of declarative memory in attention-deficit/hyperactivity disorder. Sleep Med 2011;12:672–9.
[32] Csabi E, Benedek P, Janacsek K, et al. Declarative and non-declarative memory consolidation in children with sleep disorder. Front Hum Neurosci 2015;9:709.
[33] Beebe DW. Neurobehavioral morbidity associated with disordered breathing during sleep in children: a comprehensive review. Sleep 2006;29:1115–34.
[34] Montgomery-Downs HE, Gozal D. Snore-associated sleep fragmentation in infancy: mental development effects and contribution of secondhand cigarette smoke exposure. Pediatrics 2006;117:e496–502.
[35] Ednick M, Cohen AP, McPhail GL, et al. A review of the effects of sleep during the first year of life on cognitive, psychomotor, and temperament development. Sleep 2009;32:1449–58.
[36] Bennet L, Walker DW, Horne RSC. Waking up too early – the consequences of preterm birth on sleep development. J Physiol 2018;596:5687–708.
[37] Heindel JJ, Vandenberg LN. Developmental origins of health and disease: a paradigm for understanding disease cause and prevention. Curr Opin Pediatr 2015;27:248–53.

[38] Thorpe K, Staton S, Sawyer E, et al. Napping, development and health from 0 to 5 years: a systematic review. Arch Dis Child 2015;100:615–22.
[39] Gomez RL, Bootzin RR, Nadel L. Naps promote abstraction in language-learning infants. Psychol Sci 2006;17:670–4.
[40] Hupbach A, Gomez RL, Bootzin RR, et al. Nap-dependent learning in infants. Dev Sci 2009;12:1007–12.
[41] Giganti F, Arzilli C, Conte F, et al. The effect of a daytime nap on priming and recognition tasks in preschool children. Sleep 2014;37:1087–93.
[42] Kurdziel L, Duclos K, Spencer RM. Sleep spindles in midday naps enhance learning in preschool children. Proc Natl Acad Sci U S A 2013;110:17267–72.
[43] Lukowski AF, Milojevich HM. Sleeping like a baby: examining relations between habitual infant sleep, recall memory, and generalization across cues at 10 months. Infant Behav Dev 2013;36:369–76.
[44] Chaput JP, Gray CE, Poitras VJ, et al. Systematic review of the relationships between sleep duration and health indicators in the early years (0-4 years). BMC Public Health 2017;17:855.
[45] Franco P, Kato I, Richardson HL, et al. Arousal from sleep mechanisms in infants. Sleep Med 2010;11:603–14.
[46] Lijowska AS, Reed NW, Chiodini BA, et al. Sequential arousal and airway-defensive behavior of infants in asphyxial sleep environments. J Appl Physiol (1985) 1997;83:219–28.
[47] Hirshkowitz M, Whiton K, Albert SM, et al. National Sleep Foundation's updated sleep duration recommendations: final report. Sleep Health 2015;1:233–43.
[48] Blair PS, Humphreys JS, Gringras P, et al. Childhood sleep duration and associated demographic characteristics in an English cohort. Sleep 2012;35:353–60.
[49] Plancoulaine S, Lioret S, Regnault N, et al. Gender-specific factors associated with shorter sleep duration at age 3 years. J Sleep Res 2015;24:610–20.
[50] Hirshkowitz M, Whiton K, Albert SM, et al. National Sleep Foundation's sleep time duration recommendations: methodology and results summary. Sleep Health 2015;1:40–3.
[51] Blondel B, Lelong N, Kermarrec M, et al. National coordination group of the national perinatal S. Trends in perinatal health in France from 1995 to 2010. Results from the French national perinatal surveys. Journal de gynecologie, obstetrique et biologie de la reproduction 2012;41:e1–15.