

## Review Article

# Sleep and Behavioral Disorders in School Age Children that were Born Preterm and with Very Low Birth Weight

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**Submitted:** 05 March 2020

**Accepted:** 17 March 2020

**Published:** 19 March 2020

**ISSN:** 2379-0822

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**OPEN ACCESS****Keywords**

• Sleep; Prematurity; Actigraphy; Behavior, Low birth weight

**Abstract**

**Objective:** To verify sleep characteristics in school age children that were born preterm and its association to behavioral disorders.

**Design:** Cross sectional study.

**Setting:** former patients from a Neonatal Intensive Care Unit.

**Patients:** 25 children aged between 6 and 9 years, from low socioeconomic status, who were born premature and with birth weight < 1.500 g, matched to a control (full-term) group.

**Interventions:** cognitive evaluation, sleep and behavior scales, actigraphy.

**Main outcome measures:** By actigraphy and sleep diary (24 hours/3 nights), total sleep time (TST) (normal > 9 hours), sleep efficiency (SE) (normal > 90%), night awakenings (normal < 3 awakenings with 5 minutes duration) and sleep latency (normal < 30 minutes). In the Sleep Disturbance Scale for Children (SDSC) a total score over 39 points was considered abnormal. Child Behavior Checklist (CBCL) was indicative of behavioral disorders if scores were over 63.

**Results:** Reduced TST and SE and increased night awakenings and sleep latency were observed in preterm (68%, 60%, 64%) and full-term (72%, 70%, 75%) children, respectively. SDSC and CBCL showed abnormal scores on preterm (88%, 64%) and full-term (76%, 56%). In preterm increased night awakenings were associated to abnormal CBCL score and in full-term abnormal SDSC score with altered CBCL. Actigraphy was more sensible to identify events than parents report.

**Conclusion:** Our data did not show evidences that prematurity might impair sleep at school age, however growing in a disadvantageous environment seems to affect quality of sleep and behavioral disorders.

**INTRODUCTION**

Preterm birth, prior to the 37th week of pregnancy, is a global priority issue in public health as it accounts for about 11% of all births worldwide [1,2]. Brazil was listed, in a recent report of the World Health Organization, at the 10<sup>th</sup> place among the countries with highest rates of preterm birth. The increasing rates of prematurity and low birth weight in Brazil are associated to the increasing rates of cesarean sections and induced vaginal births [3,4].

Children born preterm are at greater risk of having neurobehavioral, cognitive (visuospatial process, sensorimotor and executive functions, and memory) [5], and social disorders, including attention deficit and behavioral and language problems [6-8]. Behavioral disorders may be present in about 40% of premature children when they reach school age [7].

Sleep in preterm neonates has a peculiar organization that

reflects the degree of cerebral maturity and presents continuous changes due to the adaptation to the extrauterine environment. Sleep quality directly influences child development and growth [9,10]. Therefore, the evaluation of sleep organization is an important resource for observing neurodevelopment [9,11].

Sleep disorders might affect 20 to 30% of the children during their first 3 years of life [12] and could enhance behavioral problems such as attention disorders, increased impulsivity, disruptive behavior and academic performance [13-15].

In developing countries, with marked inequity as Brazil, low socioeconomic conditions might aggravate biological vulnerability [16]. In a recent population-based study we have observed, in children aged 0-3 years, that low socioeconomic conditions were significantly associated to an increased rate of sleep disorders [17].

Considering the clinical and behavioral characteristics

of preterm children, the influence of sleep on cognitive and behavioral performance, and the scarcity of studies that evaluate sleep with objective measures in this population, we propose the present study. Our aim is to verify if there is an association between sleep and behavioral disorders in school age children that were born preterm and with low birth weight.

## MATERIALS AND METHODS

### Design

This cross-sectional study included children aged between 6 and 9 years who were born preterm (< 37 weeks of gestational age) and with very low birth weight (< 1500 grams) at the University Hospital São Lucas – *Pontifícia Universidade Católica do Rio Grande do Sul* (PUCRS) between January 2007 and December 2009.

### Participants

Patients were selected after review of the Neonatal Intensive Care Unit database. Two hundred and seventy-nine patients were considered eligible but after an active search we were able to identify 96 patients.

The control group included children aged between 6 and 9 years who were born full-term (gestational age  $\geq$  37 weeks), with weight appropriate for gestational age, matched by age, sex, and socioeconomic status with the case group. These patients were linked to the Pediatric Outpatient Service, whether or not born at São Lucas hospital.

The exclusion criteria in both groups were presence of neurological comorbidities, use of psychotropic drugs, school dropout, and IQ <70.

### Procedures

After the parents or guardians signed the consent form and children the assent form, a psychologist (LPR), blind to the study group, evaluated patients' cognition and executive functions with the WASI (Wechsler Abbreviated Scale of Intelligence), validated to Brazilian Portuguese [18]. Individuals with IQ < 70 were excluded, namely two in the preterm group and one in the control group. In this same interview, the parents/caregivers were instructed on the use of the actigraph and the sleep diary [19].

The actigraph devices used were the Micro Motionlogger, Software Watchware (Version 1.94.0.0 and higher), Sadeh Infant PCD ZCM algorithm, and the EMSA Actimeter, from EMSA Medical Equipment Ltd., Version 1.0.0.13. The device was placed on the non-dominant wrist for 72 hours (including 3 nights). The measured parameters were as follows: (1) total sleep time (TST) on the three nights of use of the device, excluding the night awakening periods. The average time of the three nights was used in the analysis. TST was considered normal or altered based on criteria recently published by the National Sleep Foundation [20], which states that children between 6 and 13 years should sleep between 9 and 11 hours; (2) sleep efficiency (SE): given by the TST divided by the total recording time (TRT), calculated automatically by the actigraph's statistical analysis program. SE was evaluated through two references; the standard one, that considers sleep efficient when greater than

85%, and Sadeh's, which considers sleep efficient when greater than 90% [21]. SE was considered adequate when above 90% (presence of night awakenings in less than 10% of the nocturnal sleep period) [21]. (3) Night awakenings: number of night awakenings lasting 5 minutes or more, preceded or followed by 15 minutes of uninterrupted sleep. The presence of more than 3 night awakenings, each lasting more than 5 minutes in one night's sleep, was considered abnormal [21]. (4) Sleep Latency: it was calculated manually, considering the difference between the hours recorded by the caregivers in the sleep diary from when the children lay down to the sleep onset recorded in the actigraph. It was considered normal if values were lower than 30 minutes [22]. The number of weekdays and weekends in which the actigraph was used were also evaluated.

Parents completed a sleep diary, designed by the researchers, based on a previously published model [23]. In order to evaluate the concordance between the findings of the diary and those of the actigraph the following measurements were included: (1) sleep onset time; (2) sleep end time; (3) sleep latency; (4) total sleep time (difference between assumed sleep time and awake time at night, (4) awake time at night (awake time during the night sleep period).

Caregivers also answered the Sleep Disturbance Scale for Children (SDSC) [24], the Child Behavior Checklist (CBCL) [25], and a socio-demographic questionnaire.

The SDSC consists of 26 questions to access the six most common types of sleep disorders in children aged between 6 and 15 years. The cutoff point for sleep disorders is a total score of 39. A validated Brazilian version of SDSC was used [26].

For behavioral evaluation, the Brazilian version of CBCL was used [27]. This instrument has 118 items with scales of internalization and externalization symptoms. Results of CBCL were analyzed by the Assessment Data Manager (ADM) Software [28]. Children with scores higher than 63 were classified as having clinical manifestations of behavioral disorders [25,27].

### Statistics- Information analysis

Data were entered in Excel and then exported to SPSS v. 20.0 for statistical analysis. Categorical variables were described by frequencies and percentages, and quantitative variables by mean and standard deviation. Categorical variables were associated with Fisher's exact test, or chi-square test, or chi-square test with Yates correction. The symmetry of the quantitative variables was evaluated by the Kolmogorov-Smirnov test. Quantitative variables were compared between the groups by Student's t-test for independent samples or by the analysis of variance (ANOVA) test in case of comparison between more than two categories. The median and interquartile ranges were used with 25% and 75% percentiles in the variables with asymmetric results. The Spearman correlation coefficient was also calculated. The significance level was set at 5%.

### Ethical issues

The research project was approved by the Ethics and Research Committee of PUCRS protocol number 117572/2014. Parents or guardians signed an informed consent form.

## RESULTS

From the initially 96 children identified 35 had deceased, 22 lived in cities outside greater Porto Alegre, 2 had a diagnosis of autism, 2 had a diagnosis of seizures and were on anticonvulsant medication, 1 had a history of congenital malformations, 1 was under the supervision of the Guardianship Council due to severe malnutrition, 6 did not want to participate in the study and 2 were excluded because the measured IQ was below 70. Therefore, 25 patients comprised the sample.

Table 1 shows general data characterizing the two groups under study. In both groups, children had ages between 6 and 9 years and as selected in a public hospital (users of the public national health system) equally came from lower socioeconomic classes.

Among preterm patients, the causes that led to the interruption of pregnancy were preterm labor (n = 14), preterm

ruptured membranes (n = 2), pre-eclampsia (n = 4), eclampsia (n = 1), mother on hemodialysis (n = 1), intrauterine malnutrition (n = 1), and cervical dilatation with failed cervical cerclage (n = 2).

Among the full-term patients, intercurrent events and/or comorbidities during pregnancy were: chickenpox in the first trimester (n = 1), gestational diabetes mellitus (n = 1), omphalocele (n = 1), single kidney (n = 1) and fetal bradycardia (n = 1). Three caesarean sections were performed (two of them planned and one due to lack of dilatation).

The comparison between the socio-demographic data showed that preterm children had lower birth weight (P < 0.001), lower gestational age (P < 0.001), lower APGAR score at 1 minute (P = 0.004), and lower APGAR score at 5 minutes (P = 0.037). No other statistically significant differences were found between groups.

Table 2 shows the results obtained with the sleep analysis by actigraphy and with the sleep scale. In both groups, a high prevalence of sleep disorders in SDSC, TST of less than 9 hours, and sleep efficiency of less than 90% was observed. However, the comparison between groups, in the several variables studied, did not show a statistically significant difference.

Table 3 shows the comparison between TST measured by actigraphy and declared in the SDSC and night awakenings measured by actigraphy and reported in the sleep diary. The comparison of TST between the groups and between the methods (measured by actigraphy x declared on SDSC) was similar (p=0.55). However when methods were compared within the group, actigraphy was more sensible to identify night awakenings than parents report (p<0.001).

CBCL showed behavioral changes in 64% of preterm children and in 56% of full-term children. Comparison between groups did not show significant differences in any of the domains evaluated by the scale (Table 4).

The evaluation of the possible relationship between sleep organization (measured by the actigraph) and behavioral changes showed that 75% of preterm children and 78.6% of full-term children with altered CBCL also had altered TST. In preterm children, a correlation was observed between higher number of night awakenings and altered CBCL (p = 0.031). In the control group, a correlation was observed between elevated score (> 39) in the SDSC and altered CBCL (p = 0.021) (Table 5).

## DISCUSSION

The present study aimed to verify the associations between sleep and behavioral disorders in school age children who were born preterm with very low birth weight. Children included in this study, either preterm or full-term controls, had normal cognitive functions and belonged to low socioeconomic classes. Sleep evaluation was performed using objective measures (actigraphy) and subjective measures (sleep diary and the SDSC).

The results obtained evidenced a high prevalence of sleep restriction (total sleep duration lower than the age-recommended by the National Sleep Foundation) in both the preterm and control groups, as well as low sleep efficiency and long sleep onset latency. In a recent study that evaluated sleep characteristics in Brazilian children it was also observed a 23%

**Table 1:** Characteristics of the study population.

Variables	Premature n=25	Full-term n=25	P
Male	15(60.0)	15(60.0)	1,000
Age (years)	7.4±0,8	7.1±1,0	0.170
Birth Weight (grams)	1066.0±193,6	3308.2±490,9	<0.001
Gestational Age (weeks)	28.1±2.8	39.3±1.3	<0.001
APGAR 1'	6.6±1.8	7.4±2.5	0.172
5'	8.3±1.1	9.0±1.0	0.042
Normal Childbirth	15(60.0)	19 (76.0)	0.363
Caesarean Section	10(40.0)	6 (24.0)	0.363
Complications at Child-birth	12 (48.0)	8 (32.0)	0.386
WASI	94.6±11.4	92.8±11.7	0.602
Socioeconomic status*	-	-	
A	-	-	
B	-	-	
C	1 (4.0)	1 (4.0)	0.907
D	6 (24.0)	6 (24.0)	
E	4 (16.0)	6 (24.0)	
NA	14 (56.0)	12 (48.0)	
Level of instruction of mothers**			
Complete Elementary School	3 (27.5)	5 (26.3)	0.982
Complete High School	6 (54.5)	10 (52.6)	
Graduated	2 (18.2)	4 (21.1)	
Age of Mothers (years)	37.1±6.2	35.7±8.5	0.521

OBS: WASI (Wechsler Abbreviated Scale) = mean ± sd, IBGE = n (%). LI = n (%). Quantitative variables described by mean and standard deviation and compared by Student's t-test for independent samples. Categorical variables described by n (%) and compared by Fisher's exact test or chi-square test. \* Socioeconomic status as classified by the Brazilian Institute of Geography and Statistics (IBGE), classes A and B are upper level. Na= not available as parents decline to give the information. \*\* Missing data as some parents decline to give the information.

**Table 2:** Data from sleep evaluation by actigraphy and from the sleep scale.

	Premature n=25	Full-term n=25	<i>p</i>
TST actigraph			
TST actigraph (hours), mean ± sd	8.4±1.1	8.3±1.1	0.766
TST actigraph			0.999
>9 hours	8 (32.0)	7 (28)	0.999
<9 hours	17 (68.0)	18 (72)	0.999
TST sleep scale			0.768
>9 hours	10 (40.0)	8 (32.0)	
< 9 hours	15 (60.0)	17 (68.0)	
Night awakening >3 (actigraph)	16 (64.0)	18 (75.0)	0.599
Sleep Latency Actigraph (min) mean±sd	33.7±21.6	37.6±26.4	0.574
Sleep Latency Actigraph <30 min	12 (48.0)	10 (40.0)	0.776
Sleep Latency Scale			0.928
<15 min	6 (24.0)	7 (28.0)	
15 to 30 min	11 (44.0)	9 (36.0)	
30 to 45min	4 (16.0)	6 (24.0)	
45 to 60 min	3 (12.0)	2 (8.0)	
>60 min	1 (4.0)	1 (4.0)	
Sleep Efficiency Actigraph (SE %)			
SE< 90 (Sadeh)	15 (60.0)	17 (70.8)	0.620
SE< 85	14 (56.0)	12 (50.0)	0.893
Sleep Scale Score (mean ± sd)	52.6±10.9	52.1±13.2	0.880
Sleep disorders on the scale			0.463
score ≤39	3 (12.0)	6 (24.0)	
score >39	22 (88.0)	19 (76.0)	
Week Days Actigraph	2.04±0.89	1.96±0.89	0.752
Weekends Actigraph	0.96±0.89	1.08±0.86	0.630

OBS: TST (total sleep time) = n (%), SE (sleep efficiency) = n (%), Night awakening = n (%). Quantitative data with symmetrical distribution described by mean and standard deviation and compared by Student's t-test for independent samples. Categorical variables described by n(%) and compared by Fisher's exact test.

**Table 3:** Comparison between TST measured by actigraphy and declared in the SDSC and night awakenings measured by actigraphy and reported in the sleep diary.

Instrument (TST/ Night Awakenings)	Premature N=25	Full Term N=25	Premature + Full Term N=50	<i>p</i>
TST >9 hours N (%) (actigraph)	8 (32)	7 (28)	-	0.999
TST > 9 hours N(%) (SDSC)	10 (40)	8 (32)	-	0.768
TST >9 hours TST <sub>s</sub> > 9 hours N(%) (actigraph)	-	-	7 (14,3)	0.338
TST <9 hours TST <sub>s</sub> < 9 hours N(%) (actigraph)	-	-	23 (46.9)	0.338
Night Awakenings (actigraph) (median, interquartile range)	(4, 2 -5.17)	(3.83, 2.75 - 4.92)	-	0.748*
Night Awakenings (sleep diary) (median, interquartile range)	(0, 0 - 0.33)	(0.33, 0 - 0.33)	-	0.251*

\*Mann Whitney test, TST<sub>a</sub>: Total Sleep Time (Actigraph), TST<sub>s</sub>: Total Sleep Time SDSC

prevalence of sleep disorders in 4-12 years group and 65% had inadequate bedtime routines such as sleep watching TV [17]. The findings of this study, although with a more restricted sample, were in agreement with that larger one (population based),

showing that sleep habits during childhood should improve in our population.

Asaka & Takada evaluated the quality of sleep in 6 preterm children using an actigraphy and sleep diary at 15 months and

**Table 4:** Behavior evaluation by CBCL.

	Premature n=25	Full-term n=25	<i>p</i>
No alterations	9 (36.0)	11 (44.0)	0.811
Internalizing symptoms	1 (4.0)	1 (4.0)	
Externalizing symptoms	8 (32.0)	5 (20.0)	
Internalizing and externalizing symptoms	7 (28.0)	8 (32.0)	

Categorical variables described by n (%) and compared by the chi-square test.

**Table 5:** Association between changes in CBCL and variables of the actigraph and of the SDSC.

	Premature			Full-term		
	Altered CBCL n=16	Unaltered CBCL n=9	<i>p</i>	Altered CBCL n=14	Unaltered CBCL n=11	<i>p</i>
Altered TST actigraph	12 (75.0)	5 (55.6)	0.394	11 (78.6)	7 (63.6)	0.656
Altered SE <90	12 (75.0)	3 (33.3)	0.087	9 (64.3)	8 (80.0)	0.653
Altered SE <85	11 (68.8)	3 (33.3)	0.115	7 (50.0)	5 (50.0)	0.999
Night Awakenings	13 (81.2)	3 (33.3)	<b>0.031</b>	11 (78.6)	7 (70.0)	0.665
Sleep Latency	38.7±24.4	25.0±12.3	0.132	38.3±31.3	36.7±20.0	0.882
Altered TST SDSC	9 (56.2)	6 (66.7)	0.691	12(85.7)	5 (45.5)	0.081
Sleep Latency SDSC			0.267			0.569
<15 minutes	5 (31.2)	1 (11.1)		4 (28.6)	3 (27.3)	
15 to 30 minutes	5 (31.2)	6 (66.7)		4 (28.6)	5 (45.5)	
>30 minutes	6 (37.5)	2 (22.2)		6 (42.8)	3 (27.3)	
SDSC total score (>39)	15 (93.8)	7 (77.8)	0.530	13 (92.9)	6 (54.5)	<b>0.021</b>

OBS: TST = n (%), SE = n (%), Night Awakenings= n (%), Sleep latency = mean ± *sd*, TST SDSC = n (%), Sleep latency SDSC= n (%), SDSC total score = n (%). Quantitative data described by mean and standard deviation and compared by Student's t-test for independent samples. Categorical variables described by n (%) and compared by the chi-square test with Yates correction. CBCL: Child Behavior Checklist.

at school age. The changes observed in sleep at 15 months did not persist in the evaluation performed at school age in both groups [29]. Even though the present study did not have a longitudinal design, the number of children evaluated was significantly higher. However, unlike the aforementioned study, we found a high prevalence of sleep disorders in both groups. The main differences between the populations of these studies are the origin (Asian vs. Latin), the socioeconomic status, and the actigraphy time. The vulnerability of the studied population might have contributed significantly to poor quality of sleep (shared rooms or beds, housing in violent neighborhoods, and lack of sleep and feeding routines).

Opposite to Asaka & Takada [29], a longitudinal study developed in Switzerland, with a larger sample of preterm and full-term neonates, using questionnaires, did not find differences on sleep behavior from birth to age 10 y, indicating that prematurity or neonatal intensive care experience does not significantly affect sleep [30].

Biggs and collaborators [31], evaluated school age children from Australia and Canada, that were born preterm, using 14 days actigraphy and questionnaire. They have observed short sleep duration and irregular sleep schedules.

This controversial results show that the type of sleep assessment might also influence on results. Using more sensible methods as polysomnography, with macro and micro

sleep architecture, it was observed mild differences in sleep organization in children aged 5-12 years born preterm as reduction of N3 and increased N2 [32].

The comparison of sleep data as measured by actigraphy or sleep diary were not significantly different between the groups, however, actigraphy was more sensitive than sleep diary when both methods were compared. This result points to a conclusion that parents observation regarding sleep are quite imprecise and although they were aware of bedtime it does not mean sleep time. The presence of insufficient records of night awakenings in the diaries or in sleep questionnaires, already described in other studies [33-35], was reproduced in our study. The fact may reflect the difficulty of the parents to perceive the moments in which the children wake up. Werner and collaborators observed that actigraphy and diary may be interchangeably used for the assessment of sleep onset but not for nocturnal wake times but found insufficient to collect information only by a questionnaire or an interview [33]. Kushnir & Sadeh, found low correlation between actigraphy and parents report regarding sleep onset and duration and night awakenings and concluded their study warning that not only clinicians but also researchers should be highly aware that parental reports may not be accurate [34]. Markovich and collaborators, using multimodal methods to evaluate sleep in school age children such as one night polysomnography, one week actigraphy, sleep diary and a questionnaire (Children's Sleep Habits Questionnaire) found

a low correlation between CSHQ subscales and applicable PSG sleep parameters. Actigraphy significantly correlated to only one CSHQ subscale regarding night awakenings [35].

The behavioral evaluation performed through the CBCL also showed a high prevalence of internalizing and externalizing signs in both groups, and some positive correlations regarding sleep alterations. It is possible that socio-cultural variables influenced this result. In a previous study by Sadeh, parents' level of education was associated with better sleep quality [21]. Recent studies have reported that parental characteristics including socioeconomic status might influence changes in sleep and in emotional behavior in children [36-38].

We can consider as limitations of this study the number of participants and the minimum acceptable period for actigraphy use (72 hours).

In conclusion, we did not find evidences suggesting that prematurity and very low birth impair sleep at school age. However, growing in a disadvantageous environment seems to affect quality of sleep and increase behavioral disorders. Further, in the premature, we have observed an association between increased night awakenings and behavioral disorders.

As data concerning the long term influence of premature birth on sleep organization is still controversial, further studies with larger samples, and with multimodal sleep evaluation sleep should be conducted.

## ACKNOWLEDGMENTS

We acknowledge gratefully Dr. Avi Sadeh for acting as an advisor in this study and for always being helpful teaching us how to use and how to interpret the actigraphy results.

1. What is already known on this topic Children born preterm are at greater risk of having neurobehavioral, cognitive and social disorders.
2. The long term influence of preterm birth on sleep organization is still a controversial subject.

## WHAT THIS STUDY ADDS

1. Prematurity and very low birth weight does not seem to influence sleep characteristics at school age.
2. Growing in a disadvantageous environment seems to increase the prevalence of sleep and behavioral disorders.
3. Sleep fragmentation correlates with increase of behavioral disorders.

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## Cite this article

Santos AA, Romanzini LP, Nunes ML (2020) Sleep and Behavioral Disorders in School Age Children that were Born Preterm and with Very Low Birth Weight. *J Sleep Med Disord* 6(1): 1099.