



## Sleep–wake patterns in preterm infants and 6 month's home environment: implications for early cognitive development

Smadar Gertner<sup>a,b,\*</sup>, Charles W. Greenbaum<sup>b</sup>, Avi Sadeh<sup>c</sup>,  
Zipora Dolfin<sup>d</sup>, Leah Sirota<sup>e</sup>, Yocheved Ben-Nun<sup>a</sup>

<sup>a</sup>Meir Medical Center, The Department of Child Development and Neuro-Pediatrics, Kfar-Saba 44281, Israel

<sup>b</sup>Department of Psychology and Levin Center for the Development of the Child and Adolescent,  
Hebrew University of Jerusalem, Jerusalem 91905, Israel

<sup>c</sup>Department of Psychology, Tel-Aviv University, Ramat Aviv, Tel-Aviv 69978, Israel

<sup>d</sup>Meir Medical Center, Department of Neonatal Intensive Care, Kfar-Saba 44281, Israel

<sup>e</sup>Golda Medical Center, Department of Neonatal Intensive Care, Petah-Tiqwa, Israel

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### Abstract

*Aims:* This study examined the relationship between early organization of sleep–wake states and developmental outcome at 6-month-old premature infants. *Study design:* This was a prospective randomized study that evaluated the sleep–wake states of healthy premature infants in the nursery environment for two successive 72-h periods, at 32 and 36 weeks gestational age. *Subjects:* Thirty-four healthy premature infants. *Outcome measures:* Three sleep–wake parameters: percent of quiet sleep, activity level and total amount of sleep, were studied with miniature activity monitors attached to the infant's ankles. The rearing environments of the infants were also assessed at 6 months of age, using the HOME Inventory. Finally, child developmental status was recorded by means of the Mental Development Index (MDI) of the Bayley Scales for Infant Development, at a chronological age of 6 months. *Results:* Lower total time spent in night sleep, higher mean level of night activity level, and a later rich home environment were all predictive of higher Bayley scores (MDI) at a chronological age of 6 months. Regression analysis indicated that early biological maturity was more strongly related to the child's developmental status than later home environment, although both contributed to the prediction. *Conclusions:* These results suggest that biological factors may be significant

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\* Corresponding author. Meir Medical Center, The Department of Child Development and Neuro-Pediatrics, Kfar-Saba 44281, Israel.

predictors early in development, whereas the impact of environmental influences increases with development. © 2002 Elsevier Science Ireland Ltd. All rights reserved.

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## **1. Introduction**

The early development of sleep–wake state organization has long been of interest in child development. It has been considered as a sensitive indicator of neuro-physiological organization in the neonatal period, and has been found to relate to future cognitive status [1–4]. Freudigman and Thoman [5] reported that full-term newborns' sleep characteristics during the first postnatal day predicted Bayley scores at age 6 months. They suggest that the first days of life challenge the immature central nervous system of the infant and the characteristics of sleep–wake patterns are therefore highly informative. Numerous studies have described relations between various parameters of sleep–wake patterns and future mental status in preterm infants. For example, Anders et al. [1] reported that sleep–wake characteristics of premature infants at term predicted Bayley scores at 6 months and 1 year of age. They suggested that infants who sleep for long quiet sleep periods early in the night and infants who sleep for longer periods uninterruptedly are more likely to obtain high scores on the Bayley mental scale 6 months and 1 year of age, respectively. Borghese et al. [4] reported that the relationship between sleep–wake parameters and later mental score may be different when measured during the preterm period as compared to the term period. They reported that at preterm period, cyclicality length was negatively related to 6 months Bayley Mental Developmental Index (MDI) scores. By contrast, at 6 months, the same cyclicality variable was positively correlated with 6 months Bayley scores. The authors also reported that quiet sleep was not found to be related to MDI scores at either age, whereas active sleep was related to such scores at both ages.

Until recently objective methods available for sleep assessment were too demanding to enable large-scale studies. The development of actigraphy—a new method for continuous monitoring of infants' sleep in their natural environment—provides a mechanism for a reliable assessment in a large sample of infants. Actigraphy has recently been established as a reliable and valid method for assessing sleep–wake patterns in adults, children, infants and newborns [6–10].

In addition to the influence of sleep–wake biological factors on mental development, the present study also addressed the issue of the environmental contribution. Several studies have now demonstrated that social factors play an important role in the cognitive development of preterm infants [2,11,12]. Moreover, there is evidence that infants who may be undergoing neurophysiological changes may also be more vulnerable to an adverse environment. Beckwith and Parmelee [2], for instance, showed a strong relation between immature EEG patterns and lower Developmental Quotient (DQ) at 4 and 8 months. Exceptional, however, were those children being reared in a consistently attentive, responsive environment, who had higher DQ scores that were equal to those infants with more mature EEG patterns.

This study addressed two questions. Can specific sleep–wake patterns in the early premature period, at 32 and 36 weeks gestational age, predict Bayley Mental Scores at 6 months? What is the relative contribution of postnatal sleep–wake patterns and home environment on prediction of 6-month mental development?

## 2. Methods

### 2.1. Subjects

Thirty-six healthy premature Israeli infants born at Sapir Medical Center, Kfar-Saba, and Golda Medical Centers, Petah-Tiqwa, during the years 1995–1996, were enrolled in a longitudinal study. Thirty-four premature infants completed all the study procedures and will be reported. The mean gestational age of the group at birth was 29.8 (SD 2.3, range 26–34). The mean birth weight was 1279 g (SD 414, range 680–2225).

Screening criteria included a stable clinical condition, no malformation or severe illness, and no use of medication that could affect sleep–wake or breathing patterns. Cerebral sonography is routinely performed in premature infants in our unit. Thus, premature infants with any degree of intra-ventricular hemorrhage were excluded.

The sample consists of 20 boys and 14 girls including 79.4% Jewish and 20.6% Arab, 5 sets of twins, and 1 triplet. Maternal education ranged from 8 to 17 years, with a mean of 12.8 years. Paternal education ranged from 8 to 18 years, with a mean of 12.9 years.

### 2.2. Procedures

Participating mothers signed informed consent forms, expressing their willingness to participate in the study, both in the nursery environment and at their homes. Data on social and educational status, race, delivery type, birth order, and maternal age at pregnancy were obtained by chart review. Infant data regarding medical treatment, age and weight were also collected.

### 2.3. Instruments

#### 2.3.1. Sleep–wake assessment

Data collection consisted of two successive 72-h sessions of activity monitoring by miniature actigraphs (AMA-32, Ambulatory Monitoring, Ardsley, NY) that were attached to each infant's ankle. Unfortunately, there are no data regarding the reliability and validity of the actigraphic assessment in preterm infants. Sleep–wake states of premature infants may partially reflect external movements, such as feeding or medical handling. In spite of such problems actigraphy is considered an objective and nonintrusive method of measuring infant sleep [7]. An overall minute-by-minute agreement rate of 95.7% was obtained during the first year of life (including newborns), between actigraphic, automatic sleep–wake scoring and parallel scoring obtained from the method of direct observation and respiration pad following the procedure described by Sadeh et al. [7]. In this study, we have used the algorithm that has been validated with the newborns [7].

The first actigraphic assessment was made upon the infant's entering a clinically stable state, at a mean gestational age of 32.9 (SD 1.3, range 30–36) and at a mean weight of 1428 g (SD 386.1, range 961–2569). The second actigraphic assessment was made approximately 4 weeks later, at a mean gestational age of 36.2 (SD 1.3, range 34–38) and mean weight of 1977 g (SD 455, range 1260–3115). The actigraphs were initialized and downloaded to a PC where all raw data were saved and analyzed. Actigraphic raw activity data files were analyzed using the ASA program for IBM compatible PC [7,8,10] (Fig. 1).

The sleep–wake state of each preterm infant was evaluated for two 72-h periods, at 32 and 36 weeks gestational age. For the present study, we distinguished between night hours and day hours, considering the fact that in the nursery environment the caregiver's handling and medical treatment are most likely to occur during daytime. Nighttime therefore may be considered as the more reliable time for assessing the premature infant's

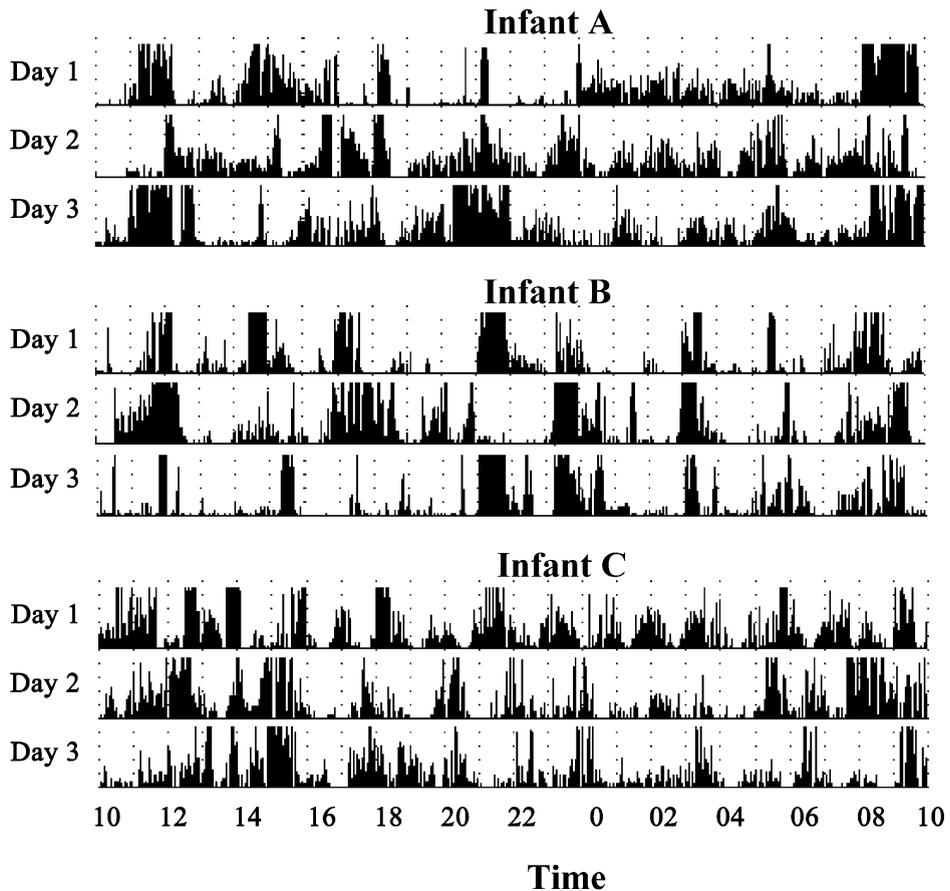


Fig. 1. Raw activity data of three preterm newborns during four successive 24-h periods each. Dark and condensed activity lines characterized wake periods. Low or absence of activity characterizes sleep periods.

movements that reflect sleep–wake pattern. For that reason the analysis was done for each 24-h period separately.

The following sleep–wake measures were derived from each (night and day) 12-h measured session, lasting from 9:00 PM till 9:00 AM the next morning: (1) sleep percent (percentage of the 12-h period spent in sleep), (2) quiet sleep (percentage of 12-h period spent in quiet sleep), (3) sleep–wake transitions (number of sleep–wake transitions), (4) mean activity level over 12 h. In addition to the 12-h summary measures, sleep–wake measures were computed for the entire 24-h period.

### 2.3.2. Home environment assessment

Home environment was assessed by a single observer at a chronological age of 6 months, using Elardo and Bradley's [13] HOME Inventory for infants. The HOME Inventory consists of 17 items measuring the infant's daily schedule, physical stimuli that are characteristic of the home and physical stimuli impinging at the infant. All items are scored in a binary (yes–no) fashion. The items are based upon observation and interview. Previous data indicate an inter-observer agreement of 89%, and an internal consistency of 0.89. Correlation between the HOME scores and concurrent and later cognitive development range from 0.4 to 0.8 indicating predictive validity [14].

### 2.3.3. Developmental assessments

The Bayley Scales of Infant Development [15,16] were administered to each infant at a chronological age of 6 months, and were scored in the standard manner. The Mental Developmental Index (MDI) was used as the measure of development in the present study. The test reliability of the MDI is 76.4, and split half reliability ranges from 0.81 to 0.93 depending on ages, and internal reliability at 6 months is 0.92 [15,16].

## 3. Results

### 3.1. Psychometric qualities of the sleep measures

To assess the stability of the sleep measures, test–retest reliability estimates for repeated measures (3 days) were calculated for each measure [17,18]. The reliability estimates for the actigraphic measures for each age (32 and 36 weeks) are presented in Table 1. As shown, the reliability estimates for total mean activity level and total sleep

Table 1  
Actigraphic sleep measures: reliability estimates \* for aggregated values over three successive days of recording.  
Analysis for each age measures

Sleep measure	32-week measure	36-week measure
Total quiet sleep	0.65	0.63
Total mean activity level	0.90	0.77
Total sleep percent	0.90	0.82

\* All estimates are significant at  $p < 0.0001$ .

Table 2

Proportion of states in 24-h period, 12-h daytime and nighttime period, and paired *t*-test comparisons between sleep–wake patterns at 32 and 36 weeks gestational age

Sleep–wake variables	32 weeks		36 weeks		<i>t</i>
	Mean	SD	Mean	SD	
Total quiet sleep (24 h)	26.00	6.60	29.49	7.13	– 2.43 *
Day quiet sleep (24 h)	24.95	6.78	28.29	7.17	– 2.33 *
Night quiet sleep (12 h)	28.16	7.47	31.87	8.58	– 2.05 *
Total activity level (24 h)	36.50	9.69	43.32	24.26	– 2.47 *
Day activity level (12 h)	40.26	11.56	48.17	17.00	– 2.25 *
Night activity level (12 h)	29.22	9.10	35.52	13.17	– 2.44 *
Total sleep percent (24 h)	86.64	6.09	81.49	8.91	3.13 *
Day sleep percent (12 h)	84.33	7.42	78.96	9.82	2.72 *
Night sleep percent (12 h)	91.14	5.54	86.38	8.83	3.01 *

\*  $<0.05$ .

percent were all above 0.70, thus, adequately reliable [17]. The reliability estimates of total quiet sleep were marginally adequate.

### 3.2. The development of sleep–wake patterns in normal premature infants

The mean and standard deviation of total quiet sleep, total activity level and total sleep percent during the 24-h period and day-and-night period are presented in Table 2.

To examine whether significant maturation of sleep–wake patterns occurred between 32 and 36 weeks, paired *t*-tests were conducted for each measure. The results are shown in Table 3. All of the states changed significantly across ages as shown in Table 2. The quiet sleep and activity level measure showed an increase, while percent sleep measures decreased over this time period.

Table 3

Pearson correlation between sleep–wake measures, and Bayley (MDI) scores

Sleep–wake variables	32-week sleep–wake measure with MDI	36-week sleep–wake measure with MDI
Total quiet sleep (24 h)	– 0.17	0.029
Day quiet sleep (24 h)	0.066	0.022
Night quiet sleep (12 h)	– 0.171	– 0.041
Total day mean activity level (12 h)	0.215	0.280
Total mean activity level (24 h)	0.259	0.317
Total night mean activity level (12 h)	0.116	0.373 *
Total sleep percent (24 h)	– 0.306	– 0.349 *
Total day sleep percent (12 h)	– 0.267	– 0.293
Total night sleep percent (12 h)	– 0.293	– 0.405 *
Total sleep wake transition (24 h)	0.225	0.164
Total day sleep wake transition (12 h)	0.133	0.093
Total night sleep wake transition (12 h)	0.330	0.238

\*  $P < 0.05$ .

Table 4  
Prediction of developmental outcome at 6 months by stepwise regression analysis \*

Independent variable	<i>B</i>	<i>t</i>	<i>p</i>
Night sleep percent (12 h period)	− 0.805	− 3.578	0.01
HOME	1.050	2.889	0.01

*B*: Regression coefficient.

*t*: *t* value for *B*.

\* Correlation coefficient  $r=0.6943$ .

### 3.3. Correlations between cognitive outcome and the two other independent variables—sleep–wake patterns and home environment

Pearson correlations were computed relating the two independent variables, sleep–wake measures at the preterm period, and home environment at 6 months old, to cognitive development at a chronological age of 6 months. The results shown in Table 3 indicate that sleep–wake patterns at 32 weeks gestational age were not significantly correlated to later cognitive development. At 36 weeks gestational age, however, the parameters of sleep–wake patterns were more strongly correlated with later cognitive development: total sleep percent (24-h period) and night sleep percent, and were significantly negatively correlated with 6 months MDI Bayley scores ( $r = -0.349$  and  $r = -0.405$ ). Night mean activity level was positively related to MDI scores.

Pearson correlations between HOME and Bayley MDI scores at 6 months revealed that home environment was positively correlated with cognitive development ( $r=0.31$ ,  $p<0.08$ ).

### 3.4. Prediction of developmental outcome

The significant predictor variables analyzed in the stepwise multiple regression of cognitive development at a chronological age of 6 months are shown in Table 4. The variables are presented using regression coefficient *B*, *t* value for *B*, and two-tailed significance level of *t*.

Only total night sleep percent at 36 weeks and HOME at 6 months were significant predictors of 6 months cognitive development as defined by the Bayley MDI, [ $F(2,22)=10.23$ ,  $p<0.001$ ].

The two variables predicted 43% of the variance of the developmental outcome variable (adjusted  $R^2=0.435$ ). The first variable, percent night sleep at mean age of 36 weeks, predicted 25% of the variance (adjusted  $R^2=0.254$ ). The second variable, HOME Inventory score, predicted 18% of the variance (adjusted  $R^2=0.18$ ).

## 4. Discussion

Before we address the specific findings of our study one major methodological limitation should be addressed. Although actigraphy has been validated with newborns

[7], it has never been validated with premature infants. Therefore, although we rely on validated sleep–wake algorithms and refer to sleep–wake measure, the phenomenon we are documenting may deviate to some extent and represent rest–activity patterns rather than sleep–wake patterns.

The results of the present study indicate that lower total time spent in night sleep, higher night mean activity level at 36 weeks gestational age, and a rich home environment, were all predictive of higher Bayley MDI scores at a chronological age of 6 months. The biological variables were slightly more strongly related to child developmental status than later home environment.

Studies describing the development of sleep–wake patterns reveal dramatic changes during the first year of life. One of the most obvious changes is the amount of time the child spends sleeping each day. The newborn infant spends two-thirds of each 24-h period asleep; by 6 months he spends half of his time asleep and half of his time awake. Sleep consolidation is another important aspect of infant's sleep development. By the age of 6 months sleep condensed into fewer periods of longer duration so that sleep periods are lengthened from 4 to 6 h [19,20]. The same developmental patterns are evidenced in preterm infants [1,21]. The present study showed a reduction in the total sleep time over 32 to 36 weeks' gestational age.

Viewed in the light of the developmental trends described above, we may explain the results of the present study as showing that early mature patterns of sleep, as indicated by decreased amount of sleep and higher activity level of the neonatal stage, are related to later (6 months) cognitive maturity.

This interpretation is congruent with those of Anders et al. [1] who reported that infants whose sleep–wake state organization demonstrates better consolidation in the first year of life are more likely to obtain high scores on the Bayley MDI scale at 6 months and 1 year of age.

The present research extends the finding of other investigators that linked the characteristic of preterm infant's sleep–wake state organization at term date with later mental status [1,2]. Our study suggests that the relation can be traced as early as 36 weeks.

The results confirm the importance of the sleep–wake system as one of the first markers of early biobehavioral organization and adaptation [19,22,23]. It also supports the concept of continuity by suggesting that during the first days of the preterm infant's life those indicators of alertness are predictive of later development outcomes.

The results of this study indicate no significant correlation between quiet sleep and later Bayley mental scores. This finding is consistent with those reported by Borghese et al. [4]. In addition, these authors, as well as we, reported a correlation between neonatal active sleep and later Bayley mental scores. The reason for the different implication of quiet sleep versus active sleep for mental development is still unclear. We suggest a possibility, based on Denenberg and Thoman's [24] argument that active sleep has a functional role in stimulating the central nervous system, thereby facilitating growth and maturation. It is possible therefore that the amount of active sleep, which reflects the maturation of the central nervous system, may be predictive of later mental development.

In addition to studying the biological factors (sleep–wake patterns) we also addressed the relation of infants' home environment to mental performance. The present results indicate that measures of sleep characteristic contribute more strongly to the prediction of

mental ability than do home environment scores. However, they also suggest that home environment may have a meaningful effect on early child development, and may thus help to overcome the developmental problems associated with low birthweight. Previous research has shown that stimulating home environments as measured by parental education and the HOME Inventory may contribute to the cognitive development of Israeli school-age children aged 7–8 born at low birthweight [25]. Other studies of infants in the USA have shown positive relations between early HOME scores obtained in the first 3 years and social and cognitive development for typical infants [26] and for low birthweight infants at 36 months [27–29]. Similar results were found for somewhat lower ages: [30], 30 months [30], and 18 months [31].

The present study indicates that the positive effects of a stimulating environment on the cognitive development of the low birthweight child may be experienced as early as 6 months. Environment contributed together with measures of neonatal sleep states to produce predictions of 6-month cognitive development as measured by the Bayley scales. These results suggest the importance of further research on early use of the HOME as a predictor of cognitive development in conjunction with measures of the child's temperament and activity level, including sleep–wake states.

In conclusion, the present study identified biological and environmental factors associated with the 6 months Bayley mental scores. More research is needed to assess the predictive value of measures derived from the preterm's sleep–wake patterns that may reflect early processes of neurobehavioral organization. The nature of the interaction effect of neuropsychological functioning in the early preterm period with later home environment needs much further study.

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