Published in final edited form as:

J Obstet Gynecol Neonatal Nurs. 2008 ; 37(6): 657–665. doi:10.1111/j.1552-6909.2008.00292.x.

Preterm Infant State Development:

Individual and Gender Differences Matter

Shuyuann Wang Foreman, PhD, RN[postdoctoral fellow]

Department of Family and Child Nursing and Biobehavioral Nursing and Health Systems,
University of Washington, Seattle, WA.

Karen A. Thomas, PhD, RN[Ellery and Kirby Cramer Endowed Professor]

Department of Family and Child Nursing, University of Washington, Seattle, WA

Susan T. Blackburn, PhD, RN[professor]

Department of Family and Child Nursing, University of Washington, Seattle, WA

Abstract

Objective—To further understand state development of preterm infants throughout hospitalization and the effects of selected infant characteristics on state development.

Design—Secondary data analysis of a two-group, experimental design study.

Setting—Two nurseries in a Northwest medical center.

Participants—Ninety-seven (97) hospitalized, medically stable, preterm infants. Fifty one (51) subjects were females.

Methods—Two hundred eighty five (285) real-time video recordings of infants performed during 4-hour interfeeding intervals. Sleep-wake states were coded at 15-second intervals.

Results—Active sleep was the dominant state across postmenstrual ages. Although not statistically significant, preterm infants showed developmental changes in state organization with increased quiet sleep, drowsy, and awake, decreased active sleep, and more defined and less diffuse states over age. A significant gender effect was found, with males having less active sleep ($p = .012$), more drowsy ($p = .03$), more awake ($p = 0.43$), less defined ($p = .002$), and more diffuse ($p = .001$) states compared with females.

Conclusion—The predominance of active sleep during the preterm period reflects level of brain maturation. The results emphasize individual variations in state organization influenced by endogenous and environmental factors. Gender differences are potential sources of individual variation.

Keywords

Gender; Preterm Infant; Sleep; State

Correspondence Shuyuann Wang Foreman, PhD, RN, Biobehavioral Nursing and Health Systems, University of Washington, Box 357266, Seattle, WA 98195-7266. yuann@u.washington.edu.

¹Infant state development reflects brain maturation and predicts later neurodevelopment.

²The large amount of active sleep during the preterm period is evidence of brain immaturity.

³Although gender differences in state organization are evident in preterm infants, little is known about the implications of these differences for developmentally based care.

Preterm infants born early with immature neurological functioning may live in the neonatal intensive care unit (NICU) for an extended period of time. From birth on, these infants face a series of challenges in various areas of development. One of the major challenges in the first months of life is state organization, the development of integrated and coordinated patterns of sleep-wake states. Stable sleep-wake organization reflects the maturation of the central nervous system (CNS) (Ardura, Andrés, Aldana, & Revilla, 1995; Blackburn, 2007; Holditch-Davis, 1998; Ingersoll & Thoman, 1999; Thoman, 2002). State development involves increasing quiet sleep, decreasing active sleep, and smooth and fewer transitions. The understanding of infant state development is a window for the assessment of the developing brain. Achieving stable sleep-wake patterns and transitions between states is a major developmental task in healthy infants in the first weeks after birth (Als, 1982, 1986).

However, the developing sleep of preterm infants is often disturbed by caregiving, medical interventions, and other environmental factors in the NICU. Although the understanding of state developmental process and its relation to neurodevelopment in preterm infants have been studied, longitudinal studies of sleep-wake states within individual hospitalized preterm infants are rare. Reasons for this knowledge gap include heterogeneous characteristics of preterm infants and the difficulties in conducting long-term studies (Holditch-Davis & Edwards, 1998a; Holditch-Davis, Scher, Schwartz, & Hudson-Barr, 2004; Ingersoll & Thoman, 1999).

The effect of preterm infant characteristics on sleep-wake organization is still unclear. In particular, very little research has explored gender-specific differences in infant state organization, and the findings are controversial (Bach, Telliez, Leke, & Libert, 2000; Holditch-Davis et al., 2004; Hoppenbrouwers et al., 2005; Thordstein, Lofgren, Flisberg, Lindecrantz, & Kjellmer, 2006). The purpose of this secondary analysis was to describe the development of state organization in preterm infants and the contribution of selected infant characteristics (gestational age (GA), birthweight, gender, postmenstrual age, and postnatal age) to state organization. Understanding preterm infants' state organization is crucial in the assessment of their behaviors and implementation of individualized developmental care.

Background

Sleep-wake states are part of the language an infant uses to express internal needs in response to external events. State organization involves complicated mechanisms that rely on the coordination of different body systems, including physiological, biochemical, and neurobehavioral systems (Rechtschaffen & Siegel, 2000; Thoman, 2002). With the maturation of state organization, healthy infants are more competent in interacting with caregivers and the environment (Vandenberg, 2007). Infants present clearer behavioral cues and use changing state as a strategy to regulate themselves under stressful circumstances (Thoman, 1999). Preterm infants, however, are born early, the CNS is immature, and state organization is limited. This is reflected in the instability of preterm infant sleep-wake states. Consequently, these infants are at high risk of later neurological problems (Barnard, 1973; Thoman, 1999; Holditch-Davis, Blackburn, & Vandenberg, 2003). In addition, the stressful and overwhelming environment in the NICU may lead to sensory overload and interfere with the frail infant's neurodevelopment (Blackburn, 1998; Holditch-Davis, Blackburn, et al., 2003), resulting in state disorganization.

Sleep-wake patterns of preterm and normal full-term infants are distinct from adults (Graven, 2006; Holditch-Davis, Blackburn, et al., 2003; Rechtschaffen & Siegel, 2000). Direct behavioral observation is the most commonly used method in identifying infant states because of its reliability and efficiency (Bertelle, Sevestre, Laou-Hap, Nagahapitiye, & Sizun, 2007). According to Brazelton and Nugent (1995), infant states are defined according

to body activity levels, eye opening and closing, eye and facial movements, regularity of respiration, vocalizations, and responsiveness to internal and external stimuli. Sleep states are categorized as quiet (deep) sleep and active (light) sleep. Awake state is comprised of four stages: drowsy, quiet alert, active alert, and crying. Drowsy stage is often viewed as the transition between sleep and wake states.

Studies have demonstrated the general patterns of sleep-wake state development in both preterm and full-term infants during the first year of life. Sleep development is categorized by increased quiet sleep, decreased active sleep, increased awake (Booth, Leonard, & Thoman, 1980; Holditch-Davis & Edwards, 1998a, 1998b; Holditch-Davis, Brandon, & Schwartz, 2003; Holditch-Davis, et al., 2004; Hoppenbrouwers et al., 2005; Mirmiran, Maas, & Ariagno, 2003), smoother transitions between wake and sleep, and increased ability to sustain sleep periods with increased age (Anders, 1979; Anders & Keener, 1985). The quantity and quality of sleep states differ between preterm and full-term infants. Additionally, preterm infant sleep-wake states differ across postmenstrual age. In more premature infants, there are periods of undifferentiated sleep, called transitional sleep or indeterminate sleep (Parmelee, Wenner, Akiyama, Schultz, & Stern, 1967). The presence of undifferentiated sleep is evidence of immature neurologic function.

Overall, preterm infants' sleep is often identified by lack of sleep cycling, shortened sleep periods, undifferentiated sleep states, and short episodes of quiet sleep compared with full-term infants (Ardura et al., 1995). Active sleep is a more primitive state than quiet sleep (Roffwarg, Muzio, & Dement, 1966). Active sleep comprises more than 70% of the sleep time of infants prior to 30 weeks gestation (Holditch-Davis, 1990; Zaiwalla & Stern, 1993); then decreases to around 50% at term (Zaiwalla & Stern, 1993). On average, infants spend less than 20% of the time in quiet sleep during the preterm period. The distribution of awake states remains minimal through the preterm period (Holditch-Davis, 1990). Because of these differences in sleep-wake development, GA, postmenstrual age, and postnatal age are important variables. Birthweight is significantly related to quiet sleep (Ingersoll & Thoman, 1999). In particular, infants with higher birthweight exhibit more organized quiet sleep (Holditch-Davis & Edwards, 1998a; Holditch-Davis, Edwards, & Helms, 1998).

In addition to measures of age, gender is an individual characteristic that may be associated with preterm infant state organization. While gender differences in sleep-wake state have been addressed by some investigators, there are other gender issues among preterm infants. Research has reported gender disparity in the neurodevelopmental outcomes of extremely preterm infants. Females have reduced risks of death and need for intensive care during the hospital stay. They are also more likely to have a favorable outcome with intensive care and reduced risks of adverse neurodevelopmental outcomes (Hintz et al, 2006; Tyson, Parikh, Langer, Green, & Higgins, 2008). Although state organization and neurodevelopment are closely interrelated, the gender effect on preterm infants' states has not received much research attention.

The evidence is limited, but some studies revealed state-related gender differences in preterm infants (Bach et al., 2000; Hoppenbrouwers et al., 2005; Korner et al., 1988). One study found females spending less time asleep, more time awake, and less waking activity throughout the early preterm period (Korner et al., 1988). Another study showed males having less sleep, more active sleep and less quiet sleep, and more frequent waking after sleep onset (Bach et al., 2000). Because of these differences, the effect of gender on preterm infants' state requires additional study to understand its potential influence on developmental outcomes and to plan individualized developmental care based on gender-related state differences.

Methods

Design

The current study was a secondary analysis of data from a previous study described in Table 1. The current project was a descriptive and exploratory study of state organization of preterm infants and its relation to selected characteristics of these infants (GA, birthweight, gender, and postmenstrual age and postnatal age at observation). Both the original and current studies were approved by university and hospital internal review boards.

Sample

Selection criteria for the secondary analysis were 1) premature infants (GA of 37 weeks or lower), 2) having at least one set of scored videotape data, and 3) having complete demographic data at the entry and exit of the original study. Ninety-seven of the 106 preterm infants from the original study met the criteria. Two hundred eighty-five video recordings from these 97 infants were analyzed and video recording was the unit of analysis for portions of this report. The sample demographics for the secondary analysis are described in Table 2. The infants entered the original study at postnatal age of 2 to 38 days and postmenstrual age of 27 to 38 weeks, and were videotaped at 31 to 39 weeks postmenstrual age. Birthweights ranged from 890 to 3630 grams. Fifty-one (52.6%) infants were females. All available videotapes were analyzed with a median of two tapes per subject. Scheduling conflicts, early unanticipated discharge, care disruptions, and poor tape quality prevented use of some recordings.

Measures

Infant Characteristics—The infant characteristics studied included GA, birthweight, gender, postmenstrual age and postnatal age at observation. GA was determined by consensus based on three measures of GA (i.e., the mother's last menstrual period, the Ballard scoring system, and ultrasound with birthweight consistent with age).

Infant State—In the original study, infant sleep-wake states were coded based on the 13-states scoring system designed by Als (1986). Each state was defined based on respirations, eye movements, eye opening, facial expressions, gross body movements, skin color, and tonus. In addition, each state was labeled in detail as diffuse (immature) or defined (mature) state. In the original study, there was little variability in the distribution of states using the 13-states coding system, and some states had extremely few occurrences. Therefore, in the secondary analysis, the 13 states were condensed into 4 major state categories: quiet sleep, active sleep, drowsy, and awake (Thoman, 2002). These four states categories were further examined using the descriptors diffuse and defined as reported by Als (1986). Diffuse and defined indicate the maturity of the specific state.

Data Analysis

Infant characteristics and states were summarized using descriptive statistics. Differences in infant demographics between the original study's two nurseries were tested using *t* test for continuous variables and chi-square for categorical variables. There were no statistically significant differences between the nurseries; therefore data were pooled for analysis. Postmenstrual age was grouped into 2-week intervals (i.e., 31-32, 33-34, 35-36, 37-38, and 39-40 weeks postmenstrual age).

The total percent of time in each of the four states (quiet sleep, active sleep, drowsy, and awake) per recording was calculated to account for variations and recording length. Percent of time in states categorized as diffuse and defined were also calculated. The mixed general

linear (MGL) model was used to determine relations of state organization with infant characteristics. Traditionally, repeated measure linear regression models are used to study changes over several time points. However, these techniques are limited to categorical independent variables and are prone to individual differences in change over time (Curran & Muthen, 1999). The MGL model has the advantages of traditional regression models and can handle unequal variances, correlated variables, clustered data, and missing data. Moreover, the MGL model provides a more comprehensive understanding of the development of state organization in preterm infants by allowing the inclusion of covariates that differ between subjects and over time, and vary in the length of observation and duration between observations. Group, as well as individual, growth patterns can be identified (Holditch-Davis & Edwards, 1998a, 1998b).

A series of MGL models were conducted using two sets of state variables, state categories (i.e., quiet sleep, active sleep, drowsy, and awake) and maturity of states (i.e., diffuse vs. defined), as dependent variables, respectively. The other four infant variables (i.e., GA, postnatal age at observation, birthweight, and gender) were used as covariates. In addition, the nursery variable was included as covariate to assure nursery effect was not different. The final models presented the variables significantly associated with the development of state organization. Postmenstrual age at observation was included in all models.

Results

State Development over Age

The descriptive results of state distribution are shown in Table 3. In the 285 recordings, the dominate state was active sleep ($M = 85.02\%$), followed by drowsy ($M = 11.50\%$) and awake ($M = 2.91\%$). There was minimal quiet sleep with a mean of 0.56% . The total amount of quiet sleep remained minimal throughout the preterm period. In general, although not statistically significant, there was a tendency of increasing quiet sleep, decreasing active sleep, increasing drowsy, and increasing awake over postmenstrual age. There were more defined and less diffuse states with increasing postmenstrual age. The three recordings in the postmenstrual age 39-40 weeks group came from two infants, and differed in terms of state development. Their characteristics and health status were not significantly different from other infants. However, the fact that the two infants were still hospitalized at 39-40 weeks postmenstrual age, and their state development patterns were different from the rest of the group suggested there might be some other underlying health problems not evident in the information available. The decision was made to omit these two outlying infants from the remaining analysis.

State Organization and Infant Characteristics

Because GA and postnatal age at observation were highly correlated ($r = -0.81$), only GA was included in the MGL analysis. The results of 282 recordings are shown in Table 4. The variables without significant results were omitted from the final models except postmenstrual age at observation, which was retained to examine developmental effect. No significant effects of GA, postmenstrual age at observation, and birthweight on state organization variables were discovered. There was a significant gender effect in the active sleep, drowsy, awake, defined, and diffuse states. The data suggest that compared to female infants, male infants showed 4.88% less active sleep, 3.50% more drowsy, 1.51% more awake, 4.70% less defined, or 4.61% more diffuse states while other variables held constant. The model of state organization was: $Y = \alpha + \beta_1 (\text{Postmenstrual age} - 35.30) + \beta_2 (\text{GA} - 32.72) + \beta_3 (\text{Birthweight} - 1958.62) + \beta_4 \text{Gender} + \beta_5 \text{Nursery} + \epsilon$, in which Y was individual states, α was intercept, β was parameter, and ϵ was standard error. For example, a female infant who was born at 32.72 weeks GA with birthweight of 1958.62 grams, when

observed at 35.3 weeks postmenstrual age in the intervention nursery, would have 88.41% of active sleep during the observation. A male infant with the same GA, postmenstrual age at observation, and intervention, would have 83.53% of active sleep during the observation. Individual infants varied significantly in their initial state status (intercept) except for quiet sleep.

No gender differences were shown in the GA and postmenstrual age at observation. Therefore, the gender effect on state organization was independent of age influence. The state variables of female infants did not show variation over postmenstrual age. In male infants, state distribution changed slightly by a decrease in active sleep, and an increase in drowsy and awake, and more mature (defined) states were shown over postmenstrual age. However, no significant interaction effect between postmenstrual age at observation and gender was discovered.

Discussion

Unlike most reports in previous literature, this study did not reveal statistically significant evidence of state change from preterm to near-term age. Quiet sleep, drowsy, and awake showed a slight increase and active sleep slightly decreased with age during the preterm period. Quiet sleep remained minimal and the majority of the time was spent in active sleep during the preterm and near-term period. Previous studies found significant changes in the state distribution over the preterm period with reduced active sleep, and increased quiet sleep and awake (Holditch-Davis, Brandon, et al., 2003; Holditch-Davis et al., 2004; Hoppenbrouwers et al., 2005). Hoppenbrouwers et al. showed improvement of sleep architecture in preterm infants from 34 to 53 weeks postmenstrual age. Both quiet sleep and active sleep showed significant maturational changes over postmenstrual age. Similarly, Korner et al. (1988) documented significant state changes from 32 weeks postmenstrual age to term age with decreasing sleep and drowsiness, and increasing awake time.

A study by Mirmiran et al. (2003) of 373 two-hour behavioral observations of 96 preterm infants (gestational age < 30 weeks) every two weeks from 30 to 40 weeks postmenstrual age showed significant increase in quiet sleep and wakefulness, and a decrease in undifferentiated sleep as well as a decrease in diffuse sleep states. In the current study, however, quiet sleep was minimal and active sleep decreased somewhat, and there was a slight decrease in diffuse states across the time period studied. The percentage of immature (diffuse) states exhibited in younger infants in the current study was much less than in the work of Mirmiran et al. Differences in coding systems among studies could potentially lead to dissimilar findings. Infant state is also highly related to environmental stimulation, and differing nursery environments could alter results. Infant health status could impact state development and influence results. In addition, the exposure to different temperature in the environment alters sleep structure, in particular, warmer temperatures produced by swaddling may alter active sleep (Gerard, Harris, & Thach, 2002).

Findings concerning preponderance of active sleep and maturity of states are consistent with earlier research. Similar to Hoppenbrouwers et al., (2005), in the current study, younger preterm infants had more immature states than older infants, and the percentage of immature states decreased with development. However, preterm infants continue to exhibit significantly more disorganized state organization at 42 weeks postmenstrual age compared to full-term infants (Hoppenbrouwers et al., 2005). Therefore, premature birth influences neurobehavioral organization and state development beyond the preterm period. The results in the current study suggest that gestational age of 32 weeks might be a turning point for the maturity of distinct state behaviors. Preterm infants under 32 weeks exhibit minimal state

organization due to brain immaturity (Mirmiran, 1995). Infant sleep-wake states are increasingly distinct after 32 weeks.

A variety of behavioral coding systems have been used to study preterm infant sleep-wake states. The coding system used in the current study may have overestimated active sleep because a conservative approach was taken. When infants showed mixed signs of active sleep and quiet sleep, periods were coded as active sleep. Video recordings of preterm infants may be problematic. The image may be unclear, the infant may move away from the camera, and swaddling may obstruct the face.

The current study agreed with the general findings of previous research about the development of states from early life: a much higher percentage of time in active sleep and lower amount of time in quiet sleep or awake if present (Peirano, Algarin, & Uauy, 2003), and more immature states presented (Hoppenbrouwers et al., 2005; Mirmiran, 1995). Nevertheless, the high proportion of active sleep during the preterm and near-term periods documented in the current study corresponds with the role of active sleep on brain development during the preterm period that has been discussed for decades. The high proportion of time spent in active sleep during the preterm period parallels the critical period of CNS development (Blackburn, 1998; Mirmiran et al., 2003). Neural activity is evident during sleep (Graven, 2006). REM (i.e., active sleep) sleep during fetal and neonatal periods plays an important role in promoting brain maturation (Graven, 2006; Mirmiran, 1995; Mirmiran & Ariagno, 2003).

Compared to results from previous studies, in the current study, the infant characteristics of GA, postmenstrual age at observation, and birthweight were not strong influences on state organization. Again, the coding system employed likely contributed to this finding although similar findings have been found by other investigators (Holditch-Davis & Edwards, 1998a; Holditch-Davis et al., 2004). While Holditch-Davis et al. also discovered no significant effects of infant characteristics (i.e., race, gender, and birthweight, illness severity, and medical treatments) on state development, postmenstrual age had significant influence on state development. In Holditch-Davis & Edwards' work (1998a), only postmenstrual age showed significant effect on state developmental patterns. In the current study, however, gender showed a significant effect on state variables. These findings indicated that biological factors, rather than extrauterine experiences, play a role in state development during the preterm period. The role of gender as a biological factor influencing preterm infant state deserves further attention.

Few studies have explored gender-specific differences on state organization of preterm infants. The limited studies found have shown debatable results. Some investigators (Borghese, Minard, & Thoman, 1995; Holditch-Davis et al., 2004; Hoppenbrouwers et al., 2005) did not find gender effect on the sleep development of preterm infants. In one study, at 34 and 35 weeks postmenstrual age, female infants slept significantly less, were awake more, and were in drowsy state more often. On the other hand, males were in waking activity (i.e., vigorous or diffuse motor activity) more. There was no significant gender effect in the number of state changes. The authors suggested that female infants mature earlier than male infants (Korner et al., 1988).

Bach et al. (2000) found the opposite. Compared to preterm girls, boys had significantly less sleep, tended to have more active sleep and less quiet sleep, were awake more after sleep onset, and tended to have shorter longest sleep periods. In full-term infants, earlier maturation of the CNS is shown in girls than in boys (Thordstein et al., 2006). In preterm infants, evidence shows that gender differences in the maturation of state organization do exist. However, the results in different reports suggest that the effect of gender on state

organization is still unclear. These differing findings indicate the need to continue study of gender differences in infant state development.

The findings suggest that state development varies in male and female preterm infants. Awareness of gender differences in state development and organization can be utilized in providing developmentally based care. This knowledge assists nurses in planning and implementing individualized care that incorporates gender differences in state development. For example, males have more drowsy state. Because drowsy state reflects transition between sleep and wake, male infants may require more attention to pacing of care based on state and may need additional support when transitioning between states. Because males display more diffuse (i.e., immature) states, they may require more time to recover following caregiving and return to a stable state. Also, diffuse states are harder for nurses to interpret and use to provide care that is sensitive to state organization. Developmental interventions that are sensitive to gender differences in infant state may help reduce neurodevelopmental problems which are currently more prevalent in male than female infants.

Limitations

Several limitations of the study may influence the generalizability of the results. First, the findings are limited to infants who are medically stable. Second, the measurement of sleep-wake patterns in the original study was not based on direct visual observations of state behavioral changes. Codings of preterm infants' behaviors from the video recordings might restrict the accuracy of observations due to the quality of recordings. Third, the measurement tools used in different studies make it difficult to compare the findings of state development in preterm infants. The definitions of state variables vary by investigators and study purposes (Curzi-Dascalova, Peirano, & Morel-Kahn, 1988). Therefore, it is difficult to establish normative state organization development in preterm infants. Fourth, although methodologically difficult to implement, frequent longitudinal measures of state development are desired. In the current study, design decisions limited the number of observations per infant. Finally, the use of secondary data presents several limitations. Secondary data analysis maximizes the use of a dataset, is timesaving, and is resource- and cost-effective. However, the purposes of the original study and the current study were different, and the original data were not collected specifically for the purpose of the current analysis. Therefore, the strategies of data collection were different.

Conclusion

This study identified active sleep as a major state during the preterm period, which is persistent with the current knowledge of active sleep in this stage of brain development. Preterm infants showed a tendency of increasing quiet sleep, drowsy, and awake, decreasing active sleep, and more defined and less diffuse states over age. Gender differences in state organization were evident. Males showed less active sleep, more drowsy, more awake, and more diffuse states than girls. Yet, individual variation and other perinatal risk factors remain imperfect predictors of CNS maturation and further neurodevelopmental outcomes. Additional research is needed to understand the level of influence and further describe state development in these infants. Caregiving and interventions that coordinate with individual preterm infants' state and improve quality of sleep should be a priority for assuring positive infant outcomes and promoting optimal brain development.

Acknowledgments

Supported by the Biobehavioral Nursing Training Grant, 5T32NR007106 and the Hester McLaws Nursing Scholarship from the School of Nursing, University of Washington. Secondary analysis of data was derived from research (TSNRP #N92-047) sponsored by the TriService Nursing Research Program. The information or content

and conclusions are those of the authors and should not be construed as the official position or policy of, nor should any official endorsement be inferred by, the Uniformed Services University of the Health Sciences, the Department of Defense, or the U.S. Government.

Reference

- Als H. Toward a synactive theory of development: Promise for the assessment and support of infant individuality. *Infant Mental Health Journal*. 1982; 3:229–243.
- Als H. A synactive model of neonatal behavioral organization: Framework for the assessment of neurobehavioral development in the premature infant and for support of infants and parents in the neonatal intensive care environment. *Physical & Occupational Therapy in Pediatrics*. 1986; 6:3–53.
- Anders TF. Night-waking in infants during the first year of life. *Pediatrics*. 1979; 63:860–864. [PubMed: 450522]
- Anders TF, Keener M. Developmental course of nighttime sleep-wake patterns in full-term and premature infants during the first year of life. I. Sleep. 1985; 8:173–192. [PubMed: 4048734]
- Ardura J, Andrés J, Aldana J, Revilla MA. Development of sleep-wakefulness rhythm in premature babies. *Acta Paediatrica*. 1995; 84:484–489.
- Bach V, Telliez F, Leke A, Libert JP. Gender-related sleep differences in neonates in thermoneutral and cool environments. *Journal of Sleep Research*. 2000; 9:249–254. [PubMed: 11012863]
- Barnard K. The effect of stimulation on the sleep behavior of the premature infant. *Communicating Nursing Research*. 1973; 6:12–33. [PubMed: 4499877]
- Bertelle V, Sevestre A, Laou-Hap K, Nagahapitiye MC, Sizun J. Sleep in the neonatal intensive care unit. *Journal of Perinatal and Neonatal Nursing*. 2007; 21:140–148. [PubMed: 17505234]
- Blackburn S. Environmental impact of the NICU on developmental outcomes. *Journal of Pediatric Nursing*. 1998; 13:279–289. [PubMed: 9798363]
- Blackburn, ST. Maternal, fetal, & neonatal physiology: A clinical perspective. 3rd. W.B. Saunders Company; Philadelphia: 2007.
- Booth CL, Leonard HL, Thoman EB. Sleep states and behavior patterns in preterm and fullterm infants. *Neuropediatrics*. 1980; 11:354–364. [PubMed: 7207705]
- Borghese IF, Minard KL, Thoman EB. Sleep rhythmicity in premature infants: Implications for development status. *Sleep*. 1995; 18:523–530. [PubMed: 8552921]
- Brazelton, TB.; Nugent, JK. Neonatal Behavioral Assessment Scale. 3rd. Mac Keith Press; London: 1995.
- Curran PJ, Muthen BO. The application of latent curve analysis to testing developmental theories in intervention research. *American Journal of Community Psychology*. 1999; 27:567–595. [PubMed: 10573835]
- Curzi-Dascalova L, Peirano P, Morel-Kahn F. Development of sleep states in normal premature and full-term newborns. *Developmental Psychobiology*. 1988; 21:431–444. [PubMed: 3402666]
- Gerard CM, Harris KA, Thach BT. Spontaneous arousals in supine infants while swaddled and unswaddled during rapid eye movement and quiet sleep. *Pediatrics*. 2002; 110:e70. [PubMed: 12456937]
- GravenSSleep and brain development. *Clinics in Perinatology* 2006; 33:693–706, vii. [PubMed: 16950320]
- Hintz SR, Kendrick DE, Vohr BR, Kennedy PW, Higgins RD, For The Nichd Neonatal Research Network. Gender differences in neurodevelopmental outcomes among extremely preterm, extremely-low-birthweight infants. *Acta Paediatrica*. 2006; 95:1239–1248. [PubMed: 16982497]
- Holditch-Davis D. The development of sleeping and waking states in high-risk preterm infants. *Infant Behavior and Development*. 1990; 13:513–531.
- Holditch-Davis, D. Comprehensive neonatal nursing: A physiologic perspective. 2nd. W.B. Saunders; Philadelphia: 1998. Neonatal sleep-wake states; p. 921–938.
- Holditch-Davis, D.; Blackburn, ST.; VandenBerg, K. Newborn and Infant Neurobehavioral Development. In: Kenner, C.; Lott, JW., editors. Comprehensive neonatal nursing: A physiologic perspective. 3rd. W.B. Saunders; Philadelphia: 2003. p. 236–284.

- Holditch-Davis D, Brandon DH, Schwartz T. Development of behaviors in preterm infants: Relation to sleeping and waking. *Nursing Research*. 2003; 52:307–317. [PubMed: 14501545]
- Holditch-Davis D, Edwards LJ. Modeling development of sleep-wake behaviors. II. Results of two cohorts of preterms. *Physiology & Behavior*. 1998a; 63:319–328. [PubMed: 9469722]
- Holditch-Davis D, Edwards LJ. Temporal organization of sleep-wake states in preterm infants. *Developmental Psychobiology*. 1998b; 33:257–269. [PubMed: 9810476]
- Holditch-Davis D, Edwards LJ, Helms RW. Modeling development of sleep-wake behaviors: I. Using the mixed general linear model. *Physiology & Behavior*. 1998; 63:311–318. [PubMed: 9469721]
- Holditch-Davis D, Scher M, Schwartz T, Hudson-Barr D. Sleeping and waking state development in preterm infants. *Early Human Development*. 2004; 80:43–64. [PubMed: 15363838]
- Hoppenbrouwers T, Hodgman JE, Rybine D, Fabrikant G, Corwin M, Crowell D, et al. Sleep architecture in term and preterm infants beyond the neonatal period: The influence of gestational age, steroids, and ventilatory support. *Sleep*. 2005; 28:1428–1436. [PubMed: 16335484]
- Ingersoll EW, Thoman EB. Sleep/wake states of preterm infants: Stability, developmental change, diurnal variation, and relation with caregiving activity. *Child Development*. 1999; 70:1–10. [PubMed: 10191511]
- Korner AF, Brown BW, Reade EP, Stevenson DK, Fernbach SA, Thom VA. State behavior of preterm infants as a function of development, individual and sex differences. *Infant Behavior and Development*. 1988; 11:111–124.
- Mirmiran M. The function of fetal/neonatal rapid eye movement sleep. *Behavioral Brain Research*. 1995; 69:13–22.
- Mirmiran, M.; Ariagno, RL. Role of REM sleep in brain development and plasticity. In: Maquet, P.; Smith, C.; Stickgold, R., editors. *Sleep and brain plasticity*. Oxford University Press; New York: 2003. p. 181-187.
- Mirmiran M, Maas YG, Ariagno RL. Development of fetal and neonatal sleep and circadian rhythms. *Sleep Medicine Reviews*. 2003; 7:321–334. [PubMed: 14505599]
- Parmelee AH Jr, Wenner WH, Akiyama Y, Schultz M, Stern E. Sleep states in premature infants. *Developmental Medicine and Child Neurology*. 1967; 9:70–77. [PubMed: 6031536]
- Peirano P, Algarin C, Uauy R. Sleep-wake states and their regulatory mechanisms throughout early human development. *The Journal of Pediatrics*. 2003; 143:S70–S79. [PubMed: 14597916]
- Rechtschaffen, A.; Siegel, J. Sleep and dreaming. In: Kandel, ER.; Schwartz, JH.; Jessell, TM., editors. *Principles of neural science*. 4th. McGraw-Hill, Health Professions Division; New York: 2000. p. 936-947.
- Roffwarg HP, Muzio JN, Dement WC. Ontogenetic development of the human sleep-dream cycle: The prime role of “dreaming sleep” in early life may be in the development of the central nervous system. *Science*. 1966; 152:604–619. [PubMed: 17779492]
- Thoman, EB. The breathing bear and the remarkable premature infant. In: Goldson, E., editor. *Nurturing the premature infant: Developmental interventions in the neonatal intensive care nursery*. Oxford University Press; New York: 1999. p. 161-181.
- Thoman, EB. Sleep-wake states as context for assessment, as components of assessment, and as assessment. In: Singer, LT.; Zeskind, PS., editors. *Behavioral assessment of the infant*. Guilford Press; New York: 2002. p. 125-148.
- Thordstein M, Lofgren N, Flisberg A, Lindecrantz K, Kjellmer I. Sex differences in electrocortical activity in human neonates. *Neuroreport*. 2006; 17:1165–1168. [PubMed: 16837847]
- Tyson JE, Parikh NA, Langer J, Green C, Higgins RD. Intensive care for extreme prematurity--moving beyond gestational age. *The New England Journal of Medicine*. 2008; 358:1672–1681. [PubMed: 18420500]
- Vandenberg KA. State systems development in high-risk newborns in the neonatal intensive care unit: Identification and management of sleep, alertness, and crying. *Journal of Perinatal and Neonatal Nursing*. 2007; 21:130–139. [PubMed: 17505233]
- Zaiwalla, Z.; Stern, A. The physiology of sleep in infants and young children. In: James-Roberts, I.; Harris, G.; Messer, D., editors. *Infant crying, feeding, and sleeping: Development, problems, and treatments*. Simon and Schuster; New York: 1993. p. 135-149.

Table 1**Original Study for the Secondary Data Analysis**

Purpose	To examine the effects of a modified care environment with reduced sound and lighting levels, and cycled lighting, on the developmental outcomes of high-risk infants.
Design	A two-group experimental design with repeated measures observing infants from birth to 6 months.
Setting	An experimental nursery and a standard control nursery of a hospital in the Northwest.
Sample	<i>N</i> = 120 infants (preterm infants: <i>n</i> = 106, with 50 in the experimental nursery and 56 in the control nursery). Inclusion criteria: 1) medically stable, 2) gestational age determined by Ballard scoring system, 3) anticipated hospital stay of at least 1 week, 3) birthweight appropriate for gestational age, 4) inborn, 5) at least one English-speaking parent, and 6) having none of the following conditions: mechanical ventilation, severe apnea or bradycardia, major congenital anomalies or chromosomal abnormalities, intraventricular hemorrhage $\geq$ Grade III, neurological pathology, or severe respiratory distress indicated by mechanical ventilation $\geq$ 28 days.
Procedure	Infants were videotaped on a specific day using a real-time video recorder at approximately 34 weeks postmenstrual age and again prior to discharge. Infants were recorded twice on each day during 4-hour inter-feeding intervals.
Outcome variable: Infant sleep-wake states	Infant sleep-wake states identified using a videotape coding form based on the 13-states scoring system designed by Als (1986). The 13-states coding system included: very deep sleep, deep sleep, noisy light sleep, light sleep, drowsy with more activity, drowsy, awake and quiet, hyperalert, bright alert, active, considerable activity, intense crying, and lusty crying. Infant states were scored at 15-second intervals by trained coders with inter-rater and intra-rater reliability of the coding maintained at $> .85$.

Table 2

Sample Demographics (n = 97 infants; n = 285 video recordings)

Variable	<i>n</i>	<i>M</i>	<i>SD</i>	Range
GA (weeks)	97	32.72	2.28	27.0-37.4
PNA at entry (days)	97	6.16	6.71	2-38
PMA at entry (weeks)	97	33.60	1.95	27.9-38.6
PNA at discharge (days)	97	23.79	15.89	6-73
PMA at discharge (weeks)	97	35.90	1.38	33.29-39.43
PNA at observation (days)	285	20.14	14.37	3-67
PMA at observation (weeks)	285	35.30	1.33	31.43-39.29
Birthweight (grams)	97	1958.62	549.38	890-3630
Gender: female	51 (52.6%)			
Race: Caucasian	72 (74.2%)			

Note. *M* = mean; *SD* = standard deviation; GA = gestational age; PNA = postnatal age; PMA = postmenstrual age.

Table 3

State Development over PMA Groups (Mean (SD)) (n = 285 video recordings)

	Total	Postmenstrual Age (weeks)				
		31-32	33-34	35-36	37-38	39-40
Observations (n)	285	6	125	116	35	3
Range of states						
Quiet sleep (%)	0.56 (2.96)	0.00	0.35 (1.90)	0.97 (4.16)	0.14 (0.74)	0.00
Active sleep (%)	85.02 (15.67)	88.75 (9.22)	84.93 (14.75)	84.75 (17.19)	84.52 (15.16)	97.85 (0.66)
Drowsy (%)	11.50 (12.96)	9.84 (7.24)	12.17 (12.27)	10.8 (14.39)	11.94 (11.56)	1.82 (0.85)
Awake (%)	2.91 (5.82)	1.41 (3.18)	2.55 (4.99)	3.30 (6.72)	3.40 (5.97)	0.33 (0.57)
Maturity of states						
Diffuse (%)	13.98 (10.73)	17.01 (13.09)	14.53 (11.84)	13.35 (9.94)	14.35 (8.84)	4.87 (5.55)
Defined (%)	85.66 (11.12)	82.99 (13.09)	85.30 (11.82)	85.98 (10.91)	85.54 (9.12)	95.13 (5.55)

Table 4

Results of the Mixed General Linear Model for the State Variables Over Infant Characteristics (n = 282 video recordings)

States	Predictor	Parameter (SE)	p
Quiet sleep	Intercept	0.81 (0.35)	0.022
	PMA	0.09 (0.15)	0.545
Active sleep	Intercept	88.41** (1.82)	0.000
	PMA	-0.07 (0.80)	0.931
	Gender	-4.88* (1.93)	0.012
Drowsy	Intercept	8.48** (1.51)	0.000
	PMA	-0.20 (.66)	0.762
	Gender	3.50* (1.60)	0.030
Awake	Intercept	2.37** (0.70)	0.001
	PMA	0.23 (0.31)	0.463
	Gender	1.51* (0.74)	0.043
Defined	Intercept	86.68** (1.33)	0.000
	PMA	0.35 (0.56)	0.537
	Gender	-4.70** (1.41)	0.002
Diffuse	Intercept	12.78** (1.28)	0.000
	PMA	-0.41 (0.54)	0.453
	Gender	4.61** (1.36)	0.001

Note. SE = standard error. PMA = postmenstrual age. PMA was centered at its mean 35.30 weeks. GA was centered at its mean 32.72 weeks. Birthweight was centered at its mean 1958.62 grams.

$Y = \alpha + \beta_1 (\text{PMA} - 35.30) + \beta_2 (\text{GA} - 32.72) + \beta_3 (\text{Birthweight} - 1958.62) + \beta_4 \text{Gender} + \beta_5 \text{Nursery} + \varepsilon$.

Y = individual states; α = intercept; β = parameter; ε = standard error.

*
p < .05, two-tailed.

**
p < .01, two-tailed.