Fetal & Neonatal Sleep Cycles

About this Document
This document is a resource to the course: Core Measure 4 Safeguarding Sleep, Lesson: Fetal & Neonatal Sleep Cycles.

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Fetal & Neonatal Sleep Cycles

The fourth neuroprotective core measure of the Neonatal Integrative Developmental Care Model is “Safeguarding Sleep.” Sleep is an extremely important issue for the infant in the NICU. At approximately 28 weeks’ gestation, individual sleep patterns begin to emerge characterized by rapid eye movement (REM) and non-rapid eye movement (NREM) sleep periods. These periods become constant by 36 to 38 weeks’ gestational age. REM sleep dominates in the initial sleep cycles; REM and NREM are nearly equal as the infant approaches term, and by 8 months of age NREM sleep occupies nearly 80% of sleep time (Hobson, 1995). REM and NREM sleep cycling are essential for early neurosensory development, learning and memory, and preservation of brain plasticity for the life of the individual (Graven, 2006).

Neonatal Sleep Cycles

To provide neuroprotective developmentally supportive family-centered care for high-risk infants in the Neonatal Intensive Care Unit (NICU), an understanding of the impact of behavioral and developmental issues in infants and families must exist. The term neurobehavioral “recognizes bi-directionality – that biologic and behavioral systems dynamically influence each other and that the quality of behavior and physiologic processes is dependent on neural feedback” (Lester & Tronick, 2012). Current research provides a deeper understanding of the importance of early life experience and the highly interactive influences of genetics and the environment on the developing brain.

Research has documented that sleep and established sleep cycles are necessary for the normal neurosensory and cortex development of the fetus and the newborn. A relationship exists between the quantity and quality of sleep in preterm infants and neurocognitive and socio-emotional outcomes. Sleep has important roles also in brain plasticity; the ability of brain to change its structure and function in response to environmental changes and needs. The interruption of normal sleep can lead to the modification of the expression of several genes that can reduce the brain plasticity. The preservation of natural maturational process of sleep is increasingly linked to enhanced cognitive development and a better functioning of the emotional relationship between mother and infant (Arditi-Babchuck, et al., 2009). Infants who sleep longer periods without interruptions have been found to have better performances to the cognitive scale of Bayley in the second semester of life (Bertelle, et al., 2005).

The late fetus and neonate exhibit discrete, spontaneous cyclic patterns of active sleep and quiet sleep. The preponderance of active sleep during the first postnatal months has been connected to development of the central nervous system, specifically functional competence of neuronal circuitry whereas quiet sleep has been associated with synaptogenesis (Tononi, & Cirelli, 2012). Emerging research provides increasing evidence that sleep deprivation has a negative effect on immune function (Bryant et al 2004). This information highlights the critical importance of protecting the hospitalized infant’s sleep pattern to promote wellness.

Infants in the NICU are exposed to repeated environmental stimuli causing frequent disruptions to the infant's sleep/wake cycles. Studies have found that premature infants are disturbed as many as 234 times in a 24-hour period (Altimier, Warner, Kenner & Amlung, 1999). Sleep deprivation has
been described as a major stressor in hospitalized adult intensive care patient’s, consequently, as sleep is the predominant behavioral state for infants, providing an environment of care that promotes sleep may also reduce stress for the hospitalized infant (Weinhouse & Schwab 2006). Developmentally supportive care focuses on reducing the stressors associated with intensive care; which in turn supports sleep in the critically ill hospitalized infant (Bertelle et al 2005). Recognizing the important role sleep plays in the ongoing development of the infant’s central nervous system, it is imperative that the NICU caregiver incorporates developmentally supportive care strategies into their caregiving routine to promote uninterrupted periods of sleep. Continuous bright lights (as well as loud sounds) in the NICU can disrupt sleep/wake states. Patients of any age who are trying to sleep find direct light unpleasant. Premature infants are photophobic; however, they will open their eyes with dim lights. If the light levels never change, infants never experience the diurnal rhythm necessary for development. Reducing light (and sound) levels will facilitate rest and subsequent energy conservation, and promote organization and growth.

One of the first requirements of early development is the process of acquiring the capacity to self-regulate. While in the womb, this capacity was accomplished by the mother’s body, but once born, becomes the infant’s job (Shonkoff & Phillips, 2000). The primary activity in brain development during the last trimester is synaptogenesis (neurons connecting to others neurons at an amazing rate of between one and two million connections per second), which forms the primitive neuronal pathways that are later refined by experience (Graven, 2006; Graven & Browne 2008). Synaptogenesis at this stage is endogenous (occurs spontaneously within the brain/neurosensory system in the absence of external stimulation) and forms the early brain architecture that is later refined by exogenous (external) stimuli. Endogenous synaptogenesis produces brain complexity and plasticity, only occurs during sleep, and occurs only during REM sleep after 28 week’s gestation; thus making this period essential to the process of endogenous stimulation and the development of neurosensory systems. Once endogenous neurosensory systems are developed, they are readied for exogenous stimulation. The environment of the fetus in utero and the preterm infant in the NICU requires appropriate levels of specific types of exogenous neurosensory stimuli for healthy early brain development (Graven, 2006; S. N. Graven & J. V. Browne, 2008).

Infant Sleep Patterns

Prior to 28 weeks, the only sleep state seen on EEG is an immature sleep stage termed “indeterminate sleep”. Indeterminate state and arousals are associated with less stable oxygenation and hypoxemic episodes, conditions frequently observed in this very immature population. The indeterminate sleep state is gradually replaced by the EEG-identifiable sleep states of active sleep (rapid eye movement, or REM, sleep) and quiet sleep (non-REM, or NREM). Normal sleep organization demonstrates maturation. REM sleep may initially comprise up to 75% of total sleep time in the 30-36 week infant; REM and NREM sleep are nearly equal as the infant approaches term, and by 8 months of age NREM sleep occupies nearly 80% of total sleep time. (Graven, 2006; Graven & Browne, 2008a; Maquet et al., 2003)

Sleep preservation and organization is an important determinant of infants’ developmental outcome. REM and NREM sleep cycling are essential for early neurosensory development, learning and memory, and preservation of brain plasticity (neuronal adaptability to new situations and demands) for the life of the individual (Maquet, et al., 2003). Premature infants during childhood are known to
have smaller brains than their full-term counterparts, with increased risks for problems with sensory processing, learning disorders, abstract thinking, behavior, coping, adaptability, and attention; brain “wiring” can be disturbed even in the absence of structural brain pathology (Graven, 2006). Undisturbed sleep is absolutely essential for normal development of the infant brain and sensory systems during the last trimester; interventions to protect and prolong sleep should be a top caregiving priority. Nursing care, no more task-oriented but relationship-oriented and based on infant behavioral cues, becomes fundamental (Colombo & De Bon, 2011).

The behavioral observation and instrumental inquiry provide insight about sleep activity; rest/activity cycles have been documented from the 24–32 weeks of gestational age when the infant is almost continuously in sleep (VON, 2005; Mirmiran, et al., 2003; Graven, 2006). A large amount (about 80%) of active sleep-rapid eye movement (AS-REM) is found in the youngest preterm infant and a progressive increasing of the quiet sleep-non rapid eye movement (QS-NREM) is found versus a decreasing of AS. By term the newborn sleeps only 70% of the time (50% AS, 50% QS). QS and AS are associated to a specific developmental task. AS is important in providing the early stimulation and activity requirements of the growing brain; during AS activity some organizational events occur as the topographical alignment of the somatosensory, auditory, visual system and their connection to limbic and cortex structures (Calciolari & Montirosso, 2011; Kenner, 2010; Arditi-Babchuck, et al., 2009; Graven, 2006). Learning and memory development are also dependent on normal cycling of sleep. This process needs the presence of three phases: (1) Acquisition phase that is related to the awake-state when brain accepts and stores sensory inputs from outside. (2) The pre-consolidation phase (that takes place during QS-NREM period) in which meaningful inputs (i.e. parent’s voice or smell of breast milk) are separated from interference inputs (i.e. the bright lights, pain etc.). (3) The consolidation phase (that takes place in AS-REM sleep) in which meaningful inputs are prepared for permanent storage (VON, 2005).

Sleep patterns of preterm infants undergo age-dependent maturational changes (Holditch-Davis, et al., 2004; Graven 2006). Sleep preservation is essential for the normal neurodevelopment and adequate growth of preterm infants (Graven, 2006; Tarullo et al., 2011). Quiet sleep (QS) is necessary for energy restoration and the maintenance of bodily homoeostasis, while active sleep (AS) is important for sensory input processing, memory encoding and consolidation and learning. Sensory inputs, in turn, may influence normal sleep–wake cycling. These assertions are especially true for vulnerable preterm infants during critical periods of brain development (Fifer et al., 2010). Estimated level of noise-related sleep disruptions during hospitalization was measured by Kuhn (2013) and based on the average level of exposure to sound peaks, it was estimated that preterm infants were exposed daily, outside their nursing times, to a mean (+ SD) of 126 (+86) isolated sound peaks of 5–15 dBA Signal-to-Noise Ratio (SNR). Fifty-five (+38) of these occurred during sleep. Based on the observed mean proportions of awakenings in each sleep state and each (SNR) range, preterm infants in the NICU may be awakened an average of 18 times per day after sound peaks. This means that if a newborn with a gestational age of 28 weeks is hospitalized through to week 37 PMA, it may be exposed to an average of 7936 (+5418) isolated sound peaks. Of these, 3465 (+2394) will occur during sleep, with an average of 1134 additional arousals due to isolated sound peaks of 5–15 dBA SNR during the hospitalization period. The short-term consequences of noise hazards for preterm infants may be poor oxygenation and increased daytime sleepiness during parental visits. Studies in infants emphasize the deleterious effects of sleep restriction. As sleep and sleep cycle preservation are critical for brain development, early processes of sensory development, learning and memory (Graven, 2006; Tarullo, et al., 2011; Fifer, et al., 2010), noise-related sleep disruptions may be particularly deleterious. The possible positive impact of noise protection strategies on the neuromotor outcomes of preterm infants provides further support for this argument (Abou Turk, et al., 2009).
Evidence shows that involving the family in care practices promote sleep pattern development (McGrath, 2014; Johnson et al., 2004). In the womb the fetus’s circadian rhythm development is related to cycled fluctuations of mother’s life; that are lost in the extra-uterine experience. Being next to the mother, the preterm infant is reconnected to the mother’s warmth, smell, taste and voice. Reconnecting the infant to the modulating effect of mother’s body and emotions are an important tool to protect sleep cycles and organization and to promote the infant developing and his/her long-term quality of life. (Kenner & McGrath, 2010; Johnson et al., 2004).

Maternal-newborn contact enhances organization of the infant's sleep patterns, and supports maturation of the prefrontal cortex and its ensuing effects on cognitive and behavioral control. Premature birth disrupts brain development and is associated with maternal separation and disturbances of contact-sensitive systems. An interventional study on kangaroo care by Feldman (2014) demonstrated that by 10 years of age, children receiving KC showed organized sleep, and better cognitive control. Results demonstrate the dynamic cascades of child physiological regulation and parental provisions in shaping developmental outcome and may inform the construction of more targeted early interventions.

There are differing views of infant sleep and a fundamental question of what sleep is and how it should be measured. Some researchers believe that the cortical EEG is a special electrographic measure with causal implications for sleep or wakefulness. For those who insist that our definitions of sleep and wakefulness critically depend upon cortical activity, EEG measures are mandatory. Others supports the argument for developmental correspondence between sleep–wake mechanisms in infants and adults, independent of the mechanisms responsible for producing differentiated cortical EEG activity (Blumberg & Seeike, 2010). In contrast, others view sleep as primarily a behavioral state that can and should be studied using behavioral criteria (Prechtl, 1992). Proponents of this view do not doubt the value and significance of electrographic criteria, including the cortical EEG, but they do not necessarily equate sleep states with cortical activity.

Bursts of amplitude and interrupted signal are hallmarks of premature brain function described for decades (Parmelee, et al., 1969). Although there is controversy in the literature about the timing of obvious cyclic changes between continuity and discontinuity and the relation to sleep and wake cycles, the first signs of clear cycling between discontinuity and continuity have been documented to emerge as an otherwise healthy infant reaches 29 weeks postmenstrual age (PMA) (Sisman et al., 2005). Continuity, discontinuity, and what is commonly referred to as sleep–wake cycling between the two patterns form the basis of interpretation of aEEG data. Among healthy premature infants, the brain function signal develops to reflect a primarily discontinuous aEEG pattern early in life with functional maturation to more continuous signal as the infant approaches term gestation. The pattern changes are aligned with the findings that the background EEG signal occurs as the result of neuronal firing in an oscillatory network between the thalamus and the cortex (Amzica & Steriade, 2000; Steriade, et al., 1994). With maturation brain function becomes more organized and begins to consistently cycle between periods of continuity and discontinuity, which will ultimately reflect developing sleep states. Neurologic effects of medications and physiologic therapeutics on vulnerable infants raise many research questions that could be informed by measuring brain function. Interventions such as skin to skin holding, developmentally supported positioning, or gentle parent touch are well suited to enhance brain growth and normal development. Brain function patterns would be excellent non-invasive short-term outcomes for clinical research. In practice, health care providers may be better prepared to plan caregiving to reduce interruption of sleep states; with brain function monitoring that is quantifiable. Amplitude-integrated EEG data interpretation in the context of optimizing premature infant care-giving will be made more accessible with straightforward techniques to define and gauge both continuity and discontinuity of brain function.
Lesson: Fetal & Neonatal Sleep Cycles

The human fetus spends between 20 and 22 hours of the day sleeping. The full term newborn sleeps 17 – 20 hours per day, with 50% of the sleep state spent in Active Sleep (AS) and 50% in Quiet Sleep (QS). Active sleep in the neonatal population is similar to REM sleep in the adult. Infants experience three sleep states: active sleep, quiet sleep, and indeterminate sleep.

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<th>Sleep State</th>
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| Active Sleep (AS-REM)| ■ Characterized by relative physiologic lability  
■ Associated with an increase in apnea and bradycardia (Graven et al., 2005).  
■ Associated with “CNS maturation and differentiation, consolidation of memory and learning and support for emotional behavior patterns” and is the greatest percentage of sleep for newborns (Kuhn, et al., 2013; McGrath, 2010).  
■ Characteristic activity is the typical rapid eye movements under closed eyelids, periods of irregular and regular breathing, and low-level activity, occasional startles, whimper, smiles, mouthing, and sucking behaviors  
■ Infants of 24-32 weeks gestation spend 80% of their time in AS-REM sleep (Calcilari & Montirosso, 2011).  
■ Term infant’s sleep consists of 50% AS-REM & 50 % QS (Calcilari & Montirosso, 2011). |
| Quiet Sleep (QS-NREM)| ■ Characterized by regular breathing, no evidence of rapid eye movements, relaxed facial expression, absent spontaneous motor activity, and occasional startles.  
■ Unlike REM sleep, infant arousal is decreased during this phase of sleep.                                                                                      |
| Indeterminate Sleep  | ■ As the infant transitions back and forth between sleep and wake states, he or she may demonstrate semi-open or closed eyelids with repeated blinking, variable motor activity, including startles and diffuse squirming, fussing, facial grimacing, and occasional soft, audible vocalization. |

Fetal & Neonatal Circadian Rhythms

Fetal circadian rhythm is established in utero as the fetus’s diurnal pattern is entrained by the maternal circadian rhythm. Current research suggests development of the infant’s postnatal circadian rhythm is influenced by genetic factors, brain maturation and environmental influences (Blumberg et al., 2014; Mirmiran, et al., 2003; Rivkees, 2007; Liu et al., 2007).

Some researchers believe that failure to provide day/night patterned lighting may cause a disruption in the development of the infant's natural biologic rhythms and interfere with establishment of the sleep-wake cycle (Rivkees et al 2007). The NICU infant may be exposed to bright light from several sources including overhead lights, phototherapy, procedure spotlights, and intermittent sunlight. Frequently there are fluctuations in lighting for staff needs with little regard to day and night cycles. Bright lighting in the NICU may be especially harmful to the very low birth-weight infant who has been accustomed to the dimly lit intrauterine environment. Although it is not entirely clear what effect bright lighting may have on the developing retina, it has been suggested that over stimulation may interfere with the development of the central visual system, especially during the third trimester of prenatal development when rapid differentiation occurs (Graven et al, 2006). Consequently, current evidence based research supports cycling lighting in nurseries for infants as well as staff with little harm associated with the practice (Rivkees, 2007; Liu et al., 2007). Recommendations from the consensus of Potentially Better Practices (Liu et al., 2007) are that for
32 weeks gestation and beyond: 1). Provide cycled lighting for infants: minimum of 1 to 2 h during the daytime and 2). When providing infant care, recognize the potential importance of non-visual entrainment factors for circadian entrainment. It is not clear at what time cycled lighting should begin and whether visual and visual-motor problems of prematurity are affected by lighting. Research on cycled lighting lacks long-term visual and other outcomes to support use in low birth-weight infants. Variations may begin from dim to dimmer before brightening to day / night lighting in the absence of more information. Current recommendations for lighting in a NICU are adjustable light levels of one to sixty foot-candles with reduced nighttime levels as low as 0.5-foot candles (Altimier & White, 2014).
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