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Review

Developmental changes in sleep and breathing across infancy and childhood

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EDUCATIONAL AIMS

The reader will come to appreciate:

- Normal development of sleep in early life.
- Differences in breathing and respiratory events across childhood.
- The importance of sleep and breathing as early markers of brain development.

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SUMMARY

Sleep and breathing are physiological processes that begin in utero and undergo progressive change. While the major period of change for both sleep and breathing occurs during the months after birth, considered a period of vulnerability, more subtle changes continue to occur throughout childhood. The systems that control sleep and breathing develop separately, but sleep represents an activity state during which breathing and breathing control is significantly altered. Infants and young children may spend up to 12 hours a day sleeping; therefore, the effects of sleep on breathing are fundamental to understanding both processes in childhood. This review summarizes the current literature relevant to understanding the normal development of sleep and breathing across infancy and childhood.
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Sleep and breathing begin in utero with spontaneous respiratory activity detected as early as 11 weeks (wk) and sleep as early as 25 wk gestational age (GA). Both activities are discontinuous at their onset and show a continuum of development from fetal life through childhood. Understanding the changes in sleep and breathing, and their temporal relationship is critical for the diagnosis and management of sleep related breathing problems in infancy and beyond. This review summarizes the current literature on the development of sleep and breathing across infancy and childhood.

SLEEP IN INFANCY AND CHILDHOOD

Sleep can be defined by behavioural and physiological criteria. During sleep there is behavioural disengagement resulting in unresponsiveness to the environment [1]. In addition, physiological parameters including brain activity, muscle tone, and cardiorespiratory control differ in sleep versus wakefulness. From the time sleep begins in fetal life to adulthood, dramatic changes occur in the time spent in sleep, the pattern of sleep across a 24 h period, the distribution of sleep stages, and in sleep architecture. Maturation of sleep is both dependent on, and a reflection of, the maturation of the central nervous system, with additional interactions between changes in sleep, the environment and the experience of sleep.

Sleep Terminology

There are separate systems for describing sleep stages in newborn infants and adults. In 1968 Rechtshaffen and Kales [2] published a

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manual for scoring adult human sleep describing two fundamentally different sleep states; rapid eye movement (REM) sleep and non-rapid eye movement (NREM) sleep with further subdivision of NREM into stages 1-4 based on the predominant EEG frequency pattern. In 2007 the American Academy of Sleep Medicine manual combined stages 3 and 4 sleep into a single stage N3 denoting slow wave sleep (SWS) with stage N used for NREM sleep that does not meet the staging criteria for a distinct NREM stage [3]. Anders, Emde and Parmalee [4] described three sleep states in newborn infants in a manual published in 1971. Active Sleep (AS) is characterized by low voltage irregular or mixed EEG activity, rapid eye-movements, movements, and irregular heart rate. EMG activity may be decreased or absent, consistent with REM sleep in adults. Quiet sleep (QS) is characterized by high amplitude, mixed frequency EEG and tracé alternant EEG activity, few body movements, and regular respirations as well as heart rate; features that are similar to stage N3 or SWS in adults. Indeterminate sleep (IS) is scored when features of both AS and QS are present in the same epoch. With rapid changes in sleep first few months of life, sleep in infancy and childhood demonstrate the transition between newborn and adult sleep. The American Academy of Sleep Medicine guidelines [3] suggest using the newborn criteria under 2 months of age and applying modified adult criteria beyond. When reviewing the literature, it is important to note that clinicians and researchers may continue to apply newborn sleep staging between 2-6 months of age when adult sleep features may not yet be present in all healthy infants.

The beginning of sleep

The emergence of sleep has been studied in pre-term infants and in the fetus. Both sets of data suggest that human sleep is a distinct behavioral state by 28-32 wk GA [5,6] with data supporting the presence of sleep state cycling as early as 25 wk GA. [7] The identification of distinct sleep stages occurs later; differentiation of Active Sleep (AS) and Quiet Sleep (QS) by electroencephalographic (EEG) pattern and eye movements may be possible as early as 27 wk GA [6] though AS is distinguishable in less than 3% of fetuses prior to 28 wk GA [5]. Towards the end of pregnancy, the percentage of both AS and QS sleep increase with a lower percentage of Indeterminant Sleep (IS) [5]. Together these data demonstrate that sleep, and hence the processes that control sleep, are well established prior to birth.

Changes in sleep architecture

After birth, features of mature, or adult sleep, emerge in accordance with development the central nervous system. The first major EEG feature of mature sleep to appear after birth is the sleep spindle; a transient EEG phenomenon with waves of 12-14 Hz lasting at least 0.5 seconds (s) [2]. While debate remains with regard to their function, sleep spindles are linked to memory consolidation and may serve as a physiological index of intelligence [8]. Spindles occur as early as 3-4 weeks post-natal age but are typically seen by 6-8 weeks post-natal age [9] and reflect development of thalamo-cortical structures as well as neural maturation [10]. Premature infants show earlier development of sleep spindles with respect to post-conceptual age [11] while delayed or abnormal development of sleep spindles are an early marker of structural or metabolic brain abnormalities [12,13]. Spindle length and density varies with age such that a nadir occurs around 2 years before reaching a maximum around 11 years of age [14].

Additional features characterize the transition to an adult sleep pattern. At 3 to 4 months (mo) post-term during quiet wakefulness, the majority of infants show irregular 50-100 μV, 3.5-4.4 Hz background activity over the occipital area described as dominant posterior rhythm (DPR) [15]. Similar to an alpha rhythm in older children and adults, DPR is reactive to eye closure but the effect may be transient and fade with continued eye closure [16]. The frequency of this baseline occipital rhythm gradually increases from its first appearance at 3.5 to 4.4 Hz to reach predominant alpha posterior rhythm of 9 Hz activity in 65% of 9 year (y) olds and 10 Hz activity in 65% of 15 y olds [17]. K complexes typically appear from 5 to 6 mo post-term. K complexes consist of a sharp negative (up to 200 μV) deflection followed by a slower positive deflection with the duration of the complex >0.5 s, being maximal over the frontal scalp region [2,9]. From their first appearance, K complexes increase in amplitude to reach a maximum around 3-5 y of age. Vertex sharp waves, described as a small positive spike followed by a larger negative spike, have been identified as early as 3 wk of age [15] but they become sharper with shorter duration by 24 mo and are maximal over the central midline. Beginning at 2-3 mo of age, infants show delta activity, as seen in SWS, similar to adults with. SWS is typically present by 4 to 4.5 mo post-term [9], though delta activity (i.e. amplitude >75 μV) is evident at 2-3 mo of age [18]. These progressive changes mean that it becomes possible to distinguish NREM sleep stages between 3-6 mo of age, with the majority of infants demonstrating clear differentiation of NREM sleep stages by the age of 6 mo.

Circadian pattern of sleep

The suprachiasmatic nucleus contains the circadian pacemaker and is functional before birth. The fetus shows a circadian rhythm consistent with the mother's and maternal melatonin is likely to account for this synchronization [19]. Newborn infants, however, show no independent circadian pattern of sleep before 1 mo of age [20] with sleep and wake occurring throughout the 24 h period. The development of circadian patterns, including those for wake and sleep, are influenced by environmental exposures such as feeding pattern, and the type and timing of light exposure. For example, in a study comparing infants born full and pre-term, the length of exposure to a single caregiver and light-dark cycle predicted development of a sleep-wake circadian pattern independent of the infants' full or pre-term status [21].

The wake circadian rhythm is present by 45 days of age [22] and the circadian rhythm for sleep is evident by 4-8 wk of age [21–24]. Around 5-6 wk after birth, sleep becomes more concentrated during nighttime with increasing periods of daytime wakefulness [25]. By 12-14 wk of age, a diurnal pattern is established with a long nocturnal sleep period, shorter sleep periods during the daytime (i.e. naps) and 1-3 h of wakefulness preceding the nocturnal sleep period [19]. By 6 mo of age, infants display a circadian pattern with period, amplitude, and phase activity similar to an adult. [19]

Total sleep time, sleep cycle length and sleep efficiency

Infants born at term spend 16-18 h in sleep each day. Total sleep time (TST) decreases across infancy, early childhood and adolescence (Figure 1). [26–38] Daytime sleep decreases in both number and duration in the first years of life with 82% of children older than 18 mo not taking naps on some or all days [39]. In contrast to TST, sleep cycle length, defined as the time to cycle through all sleep stages, increases from infancy through childhood; from 46 minutes in preterm infants, 69 minutes at term [40] to 85-115 minutes in children 8-12 years of age [41]. There is also change in the sleep cycle length across the night with shorter sleep cycle duration earlier compared to later in the night. This means that with increasing sleep consolidation, there are fewer but longer sleep cycles across a sleep period [25]. There is little information about changes in sleep cycle length in adolescents but adults are classically reported to have a cycle length of approximately 90 min

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