Chapter 1

Normal Human Sleep at Different Ages: Infants to Adolescents

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Key Concepts

- Sleep behavior in children must be viewed within a biopsychosocial framework; sleep structure, organization and regulation are governed by intrinsic biological processes. Children's sleep is also shaped by cultural values, parental beliefs, and social systems.

- All aspects of sleep behavior in children exhibit large variability among individuals and across cultures.

- From the newborn period through adolescence, human sleep shows enormous changes in physiology, phenomenology, and distribution.

- Newborn sleep is polyphasic. Monophasic sleep emerges in early childhood (ages 3-5 years) when naps cease to be a regular occurrence.

- Major processes in child development influence sleep behavior of preschoolers, such as the development of locomotion, cognitive processes, attachment, and autonomy. Whether sleep behaviors in young children are considered "problematic" depends a great deal on parents' perceptions and expectations.

- School children usually begin to manifest an inherent circadian sleep phase preference (e.g., evening type or "night owl" in contrast to morning type or "morning lark"). Older school aged children and adolescents typically show a lifestyle and bioregulatory sleep delay.

- Behavioral states, sleep stages and sleep electrophysiology change as a function of age: In the first 6 months after birth, *rapid eye movement sleep* (REMS) is called *active sleep*, while *non-REM sleep* (NREMS) is termed *quiet sleep*. NREMS-REMS cycle lengthens from about 50 to about 90-110 minutes by school age. REMS accounts for about 50% of total sleep in newborns, decreasing to about 20-25% of sleep in adolescents. NREMS stages begin to emerge in the first year, with sleep spindles arising at age 4 weeks, high voltage slow waves at age 3 months, and K complexes at age 6 months.

- Sleep is a dynamic and regulated set of behavioral and physiological states and stages. Two distinct processes determine the timing of sleep and waking: a sleep-wake dependent *homeostatic process* that interacts with a sleep-wake independent, clock-like *circadian process*. Both mechanisms undergo significant modifications during development.

- A number of researchers have proposed a major role of sleep for brain maturation, development, and learning processes during childhood.

Introduction

Sleep changes as a function of age. Basic knowledge of what constitutes normal sleep patterns during childhood is a prerequisite for understanding sleep disorders in children. The goals of this section are (1) to depict normal patterns of sleep behavior as experienced by family and child, (2) to describe behavioral states, sleep stages, and sleep electrophysiology in children, and (3) to identify changes in sleep-wake (homeostatic) and circadian regulatory processes across early human development.

Two basic principles underlie normal childhood sleep:

- Sleep behavior in children must be viewed within a biopsychosocial framework; sleep structure, organization, and regulation are governed by intrinsic biological processes. Children's sleep is also shaped by cultural values, parental beliefs, and regulation of social systems.
- All aspects of sleep behavior in children exhibit large variability among individuals and across cultures.

Developmental Patterns of Human Sleep Behavior

Newborns and Infants (0 to 12 months): Sleep of newborns is distributed approximately equally across the day and night (Figure 1). After a few weeks of life, however, infants gain the ability to sustain longer episodes of sleep and waking, with sleep consolidating towards the nighttime, nocturnal sleep duration increasing (Figure 2, lower panel), and daytime sleep declining. Infants eventually begin "sleeping through the night" (i.e., sleeping at least 8 hours at night), a major developmental milestone achieved by most infants by age 6 to 9 months. Total sleep duration in the first year remains relatively constant (Figure 2, upper panel, average 14 hours per day); however, individual variability is large. For example, at age 6 months, an infant may sleep as little as 10.5 or as much as 18 hours each day.

Early childhood (12 months to 6 years): The decrease of sleep duration across early childhood (Figure 2) is a result of the reduction of daytime naps. Most children stop napping between the ages of 3 and 5 years, although cultural differences exist. Nightwakings are common in toddlers/preschoolers and may be considered a "normal" developmental phenomenon (20% wake up at least one time each night, 50% at least one night per week). Such awakenings are considered a consequence of nocturnal arousals driven by the ultradian rhythm of sleep cycles (50 to 90 minutes). Whether nightwakings become a behavioral problem depends on the child's ability to fall back asleep without parental intervention (i.e., the child is a "self soother"). Major processes in child development influence sleep behavior of preschoolers: (1) increased independent locomotion may result in parent-child bedsharing when a child awakens in the middle of the night ("reactive" co-sleeping); (2) cognitive development may produce nighttime fears as well as interests in transitional objects or sleep aids such as a pacifier, doll, blanket, and so forth, that facil-

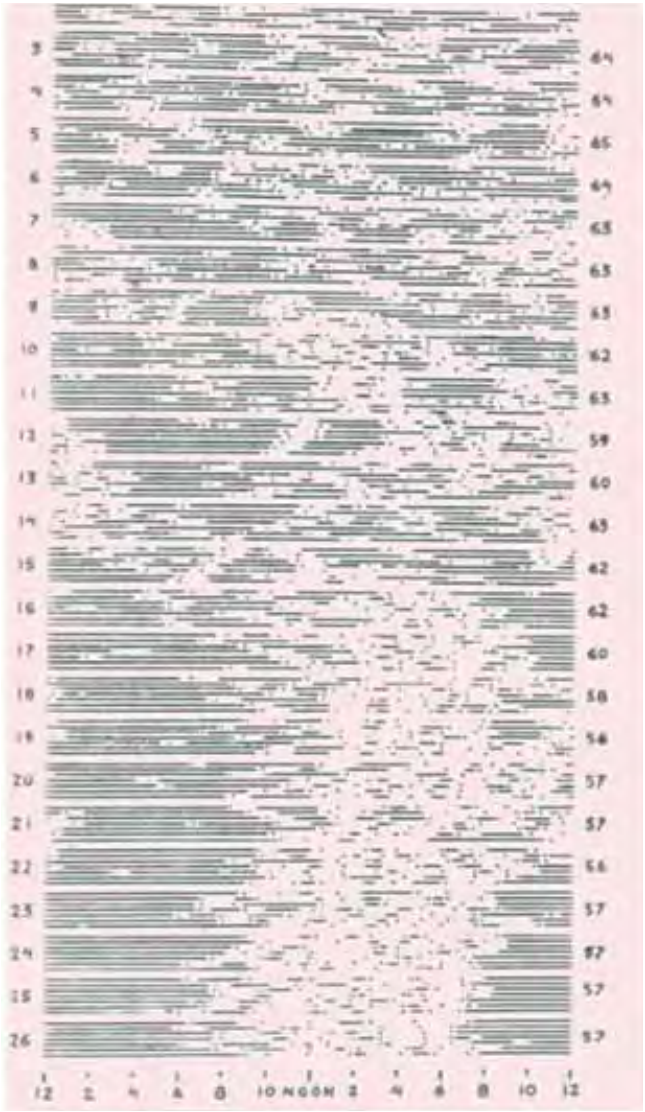

Figure 1. Development of diurnal rhythmicity in the first months after birth (Kleitman, N. Sleep and Wakefulness. University of Chicago Press: Chicago, 1963, Figure 15.2, page 137).

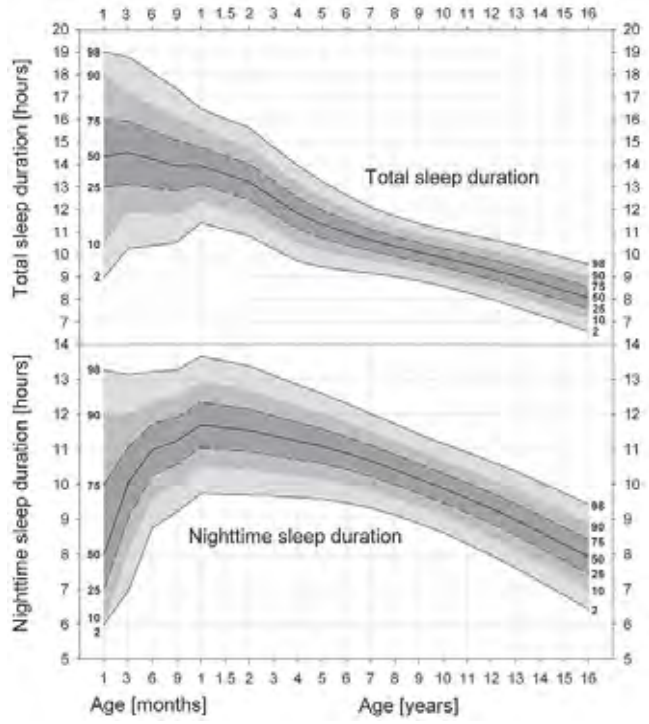

Figure 2. Percentiles of total and nighttime sleep duration (time in bed) per 24 hours (n=493, Zurich Longitudinal Studies) (adapted after Iglowstein, I., Jenni, O. G., Molinari, L., Largo, R.H. Sleep duration from infancy to adolescence: reference values and generational trends. Pediatrics 2003; 11: 302-307. © PEDIATRICS).

itate children's transitions from waking into sleep; (3) attachment issues may emerge and manifest as separation anxiety leading to frequent nightwakings and parent-child bedsharing; and (4) the toddler's drive for autonomy may be associated with frequent bedtime resistance. Whether these behaviors are considered "problematic," depends a great deal on parents' perceptions and expectations. The bedtime routine, i.e., a culturally-specific set of activities such as dressing in a particular night dress, telling stories, and singing lullabies, is often an important part of the sleep onset milieu in preschoolers. Although most EuroAmerican children sleep alone in separate rooms, the norm for children in many cultures around the world is to sleep with an adult or with a sibling ("lifestyle" co-sleeping). Climatic factors, family size, space availability, parental beliefs, and cultural preferences often condition sleeping arrangements.

School age (6 to 12 years): School children usually begin to manifest an inherent circadian sleep phase preference (e.g., evening type or "night owl" in contrast to morning type or "morning lark"). Thus, determining the "normal" bedtime for all children at a specific age is not possible, considering the biological variation in circadian phase preference. School age is a critical time for the emergence of problematic sleep habits (e.g., arousal by evening TV watching in the bedroom). Older school aged children may begin to manifest lifestyle and bioregulatory sleep delay often coinciding with the onset of puberty.

Adolescence (12 to 18 years): While sleep duration decreases in the first 10 years of life, sleep need does not decline in the course of adolescence (around 9.25 hours on average). The most important change in adolescent sleep behavior is the delay of the sleep phase (Figure 3); thus, adolescents tend to stay up late at night and sleep late in the morning compared to preadolescents. This phase delay may result in presumed insufficient sleep during the school week and "catch-up sleep" during weekends. Explanations for the phase delay are easy to find in the changing adolescent psychosocial milieu, the teenage wishes for autonomy and independence, shifts in family configurations, peer culture and social expectations, academic demands, school culture, employment opportunities, and extracurricular activities. Maturational changes of biological sleep processes, however, are also related to sleep timing and amount during adolescence (see below).

Behavioral States, Sleep Stages and Sleep Electrophysiology During Development

Behavioral states: Behavioral states are constellations of functional patterns and physiological characteristics of sleep and wakefulness that are relatively stable and occur in a predictable manner. In the young infant, five behavioral states are defined on the basis of direct behavioral observations, sometimes accompanied by noninvasive physical measures like heart rate and motor activity: *quiet sleep, active sleep, quiet alertness, active alertness,* and *vocalization (crying).*

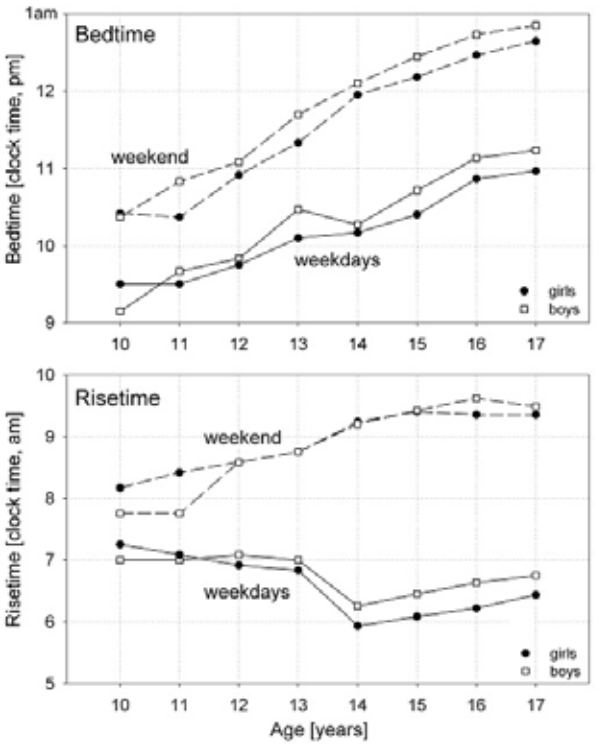

Figure 3. Weekday/weekend sleep patterns in adolescents (data source Carskadon, M.A. Patterns of sleep and sleepiness in adolescents. Pediatrician 1990; 17: 5-12.).

Sleep states: Two distinct sleep states are defined on the basis of polysomnography that monitors electroencephalographic (EEG) patterns, eye movements (EOG) and muscle tone (EMG): *REM sleep* (rapid eye movement sleep, REMS) and *non-REM sleep* (NREMS). Figure 4 illustrates the central referential EEG patterns typical of NREMS at several ages. In the first 6 months after birth, REMS is called *active sleep*, while NREMS is termed *quiet sleep*. In newborns, *quiet* and *active sleep* are often disorganized and immature (called *indeterminate or transitional sleep*). NREMS is characterized by low frequency, high voltage EEG activity, low muscle tone and absence of eye movements. An EEG pattern called tracé alternant (Figure 4) with high voltage slow activity interrupted by near electrical silence is common in the very young. Respiration patterns and heart rate are regular in NREMS. After 6 months of age, NREMS can be divided into 4 stages on the basis of distinct EEG features (Figure 4). Stage 1 NREMS occurs at transitions of sleep and wakefulness. Stage 2 is characterized by frequent bursts of rhythmic EEG activity, so-called sleep spindles (first occuring after 4 weeks of age), and high voltage slow spikes, so-called K-complexes (first appearing after 6 months). In stages 3 and 4, the EEG pattern comprises more or less continuous high voltage activity in the slowest (< 2 Hz) frequency range. EEG voltage shows a significant increase in the first year, particularly evident in NREMS. From ages 9 to 16 years, on the other hand, EEG voltages are markedly attenuated.

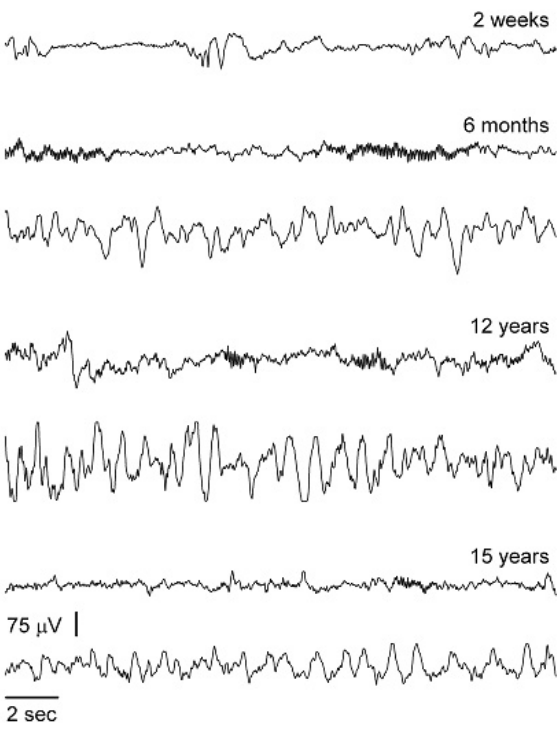

Figure 4. Illustration of EEG tracings (derivation C3/A2, 20 sec epochs) of quiet sleep/non-REM sleep at selected ages. The top tracing shows a tracé alternant pattern in a newborn infant. The bottom 6 tracings illustrate stage 2 and slow wave sleep at ages 6 months, 12 and 15 years.

REMS is characterized by high levels of desynchronized cortical EEG activity (mixed frequencies, relatively low voltage), absence of muscle tone, irregular heart rate and respiratory patterns, and episodic bursts of phasic eye movements, the hallmark of REMS. The term *active sleep* in young infants reflects frequent muscle twitches and body jerks that break through the muscle inhibition of infant REMS.

In the first months of life, infants' sleep is divided evenly (50:50) between NREMS and REMS. The proportion of REMS decreases throughout early childhood to the adolescent and adult level of about 20 to 25% of nocturnal sleep. When young infants fall asleep, the initial sleep episode is typically REMS, that is, sleep onset REM periods. After 3 months, sleep onset REM periods become replaced by the adult pattern, i.e., sleep onset NREM periods. Slow-wave sleep (SWS; NREMS stages 3 and 4) is greatest in early childhood, drops off abruptly in the course of puberty (50% decline in SWS between age 12 and 14 years, Figure 5), and further declines across the life span. This developmental pattern of SWS reflects the changing EEG amplitude that may be related to the age-specific "programmed" alterations in synaptic connectivity among neurons and changes in neuronal, neurotransmitter, or neuroreceptor properties.

Sleep cycles: NREMS and REMS alternate through the night in cycles (ultradian sleep rhythms) with a period of about 50 minutes in infancy. The period of this ultradian rhythm gradually lengthens through childhood achieving mature period length of about 90-110 minutes around school age. SWS predominates in the sleep cycles early at night while, in the last part of the night, the proportion of REMS is increased (Figure 5).

Basic Concepts of Sleep Regulation During Early Human Development

Sleep is a dynamic and regulated set of behavioral and physiological states and stages. Current theoretical models describe two intrinsic regulatory processes that determine the timing of sleep and waking (Figure 6). A sleep-wake dependent *homeostatic process* accounts for an increase of sleep pressure as waking is extended and for a recovery process occurring during sleep. This homeostatic process interacts with a sleep-wake independent, clock-like *circadian process*. The circadian mechanism has a distinct neuroanatomical locus, and molecular components have also been identified (see Section 3). The homeostatic sleep-wake process is less well defined on a neuronal basis, although the intensity of slow wave activity in the delta range during NREMS (EEG delta power) has been proposed as an electrophysiological manifestation of this process (see Section 3). This two-process model of sleep regulation accounts remarkably well for

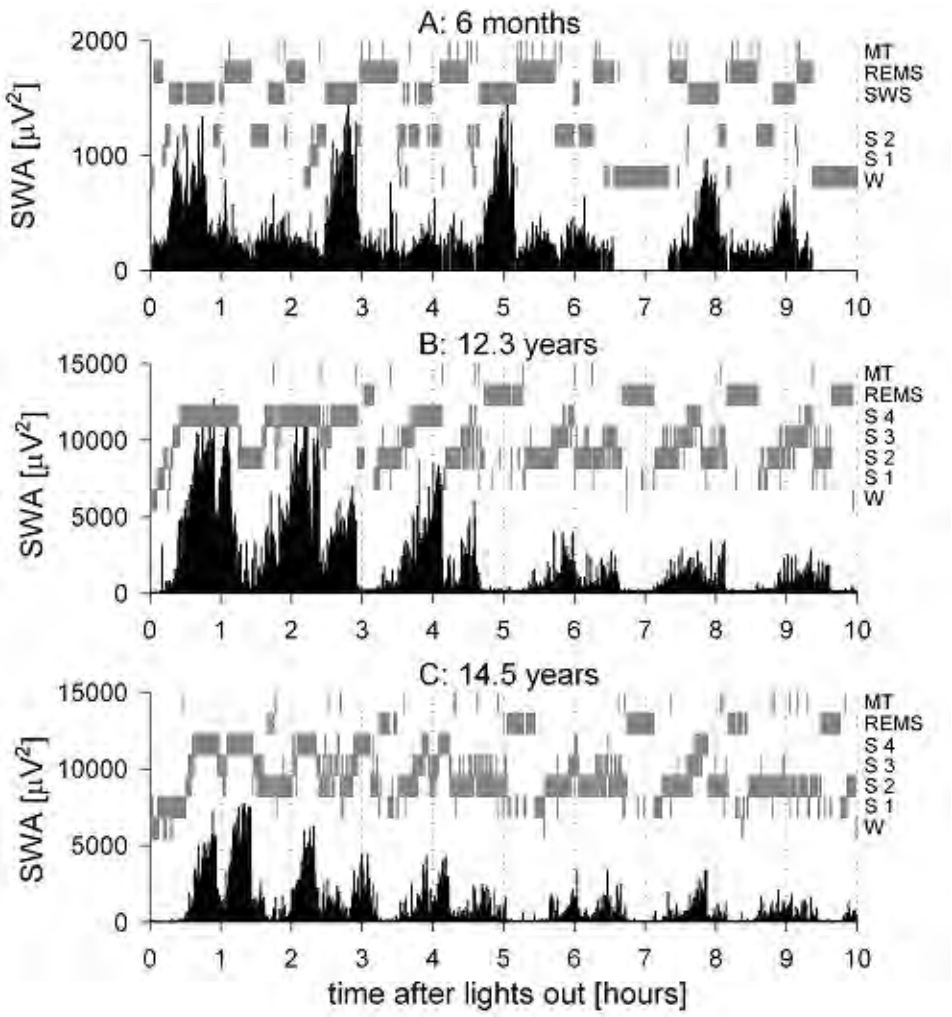

Figure 5. Visually scored sleep stages (gray bars) and time course of slow-wave activity (SWA, EEG power in the 0.6 - 4.6 Hz range) during 10-h sleep episodes at three different ages: **A**, 6 months; **B**, 12.3 years; **C**, 14.5 years. At age 6 months, stages 3 and 4 were clustered as slow wave sleep (SWS). Note the different scaling of the y-axis at 6 months. Gaps in EEG power represent periods when the headbox was disconnected (wakefulness, nursing). The same girl was recorded longitudinally at ages 12.3 (**B**, pre-pubertal stage Tanner 1) and 14.5 years (**C**, mature pubertal stage Tanner 5). MT, movement time. (Figure adapted from Jenni, O. G., Borbély, A. A., Achermann, P. Development of the nocturnal sleep electroencephalogram in human infants. Am J Physiol 2004; 286: R528-538 AND Jenni, O. G. and Carskadon, M. A. Spectral Analysis of the Sleep Electroencephalogram During Adolescence. Sleep 2004; 27(4): 774-83.). © SLEEP.

the timing of sleep in humans and a number of other mammals. Both mechanisms undergo significant modifications during development.

Development of the circadian timing system: The biological clock, located in the bilateral suprachiasmatic nuclei of the anterior hypothalamus, appears to be functional *in utero* and thus may directly control fetal behavioral rhythms. Immediately after birth, however, significant daily rhythms do not occur; that is, episodes of sleeping and waking appear randomly distributed across day and night. The circadian timing system undergoes major developmental changes within the first months after birth: at age 1 month, the 24-h core body temperature rhythm emerges; at age 2 months, infants begin to sleep more at night than during the day; at age 3 months, endogenous production of the circadian driven hormones melatonin and cortisol start to cycle in a 24-h rhythm. This early development of circadian rhythms is based on specific maturational processes of the brain interacting with social (maternal) and environmental (light-dark cycle) time cues. Guidelines by the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists (1997) have recommended the use of regular day-night cycles in perinatal care centers to improve early infant circadian organization and development.

The circadian timing system becomes mature after around 6 months of age and appears to remain relatively stable in the course of early and middle childhood, though research in this age range is limited. Several distinct changes of circadian regulation appear during puberty that influence the well-known sleep phase delay that is common for most teenagers across many societies and cultures (Figure 3). Three circadian timing mechanisms have been proposed to govern the adolescent sleep phase delay. First, intrinsic circadian phase undergoes a delay in association with puberty; thus, the correlation of pubertal stage with the circadian phase marker melatonin demonstrates that more mature children show a later timing of melatonin secretion onset and offset phases. Second, the delay of the circadian phase may be related to a lengthening of the intrinsic period of the circadian clock. Data are suggestive, but do not conclusively support this hypothesis, showing longer intrinsic period in adolescents versus adults but not across adolescent development. This finding may relate to the suggestion that a behavioral phase marker (chronotype) can mark the “end of adolescence” early in the second decade, when a reversal occurs in the trend for chronotype to delay. Third, heightened sensitivity to

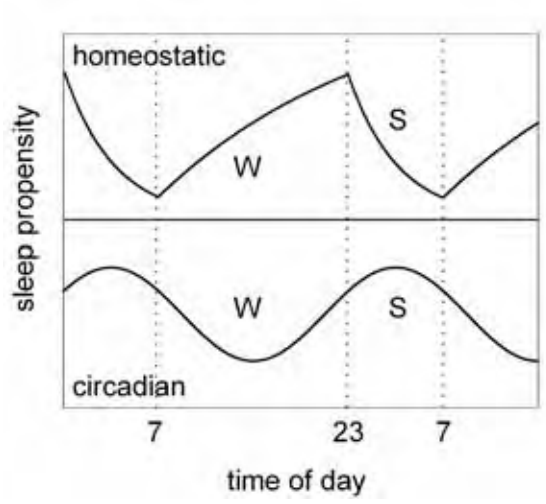

Figure 6. Schematic illustration of the two-process model of sleep-wake regulation (Carskadon, M. A., Acebo, C., Jenni, O. G. Regulation of Adolescent Sleep: Implications for Behavior. Annals of the New York Academy of Sciences 2004; 1021: 276-291, redrawn from Achermann, P. & Borbély, A. A. Mathematical models of sleep regulation. Frontiers in Bioscience 2003; 8: S683-93.). © NY ACAD SCI.

evening light or decreased sensitivity to morning light across pubertal development may also drive a sleep phase delay, though data supporting this hypothesis are minimal. In contrast to these proposed intrinsic changes to the circadian timing system, behaviorally guided changes in the timing of light exposure (e.g., by TV watching late at night) may directly interact with the phase resetting mechanism of the circadian timing system and reinforce or strengthen the phase delay tendency of teenagers.

Development of sleep homeostasis: Sleep is homeostatically regulated early in human life; short episodes of sleep deprivation in young infants lead to compensatory increases of sleep time and intensity. Because sleep loss tolerance of newborns is quite low, infants cannot sustain consolidated periods of wakefulness. Several studies suggest that the rise rate of homeostatic sleep pressure with waking during the day and its dissipation during sleep are faster in infants than in adults. Adult sleep pressure is indexed by slow-wave activity (SWA, EEG spectral power in the 0.5-4.5 Hz frequency range) while, in infants, theta activity (4.5-7 Hz) may be a marker for sleep homeostatic pressure. The age at which SWA becomes the sleep homeostatic marker is not known. We do know, however, that the effects of adolescent sleep deprivation on the sleep EEG are remarkably similar to those in young adults; the homeostatic response of SWA to sleep loss is clearly manifested in 10-year old children. The rise rate of homeostatic sleep pressure during the day is slower in mature adolescents compared to pre- or early pubertal children, which may contribute to their differences in sleep timing (i.e., the delay of the sleep phase). The nocturnal dissipation of sleep pressure (reflecting recovery processes during sleep), however, does not differ between prepubertal and mature teenagers which is in accordance with the notion that sleep need does not change in the course of pubertal maturation. Taken together, the dynamics of sleep homeostatic mechanisms appears to slow down in the course of development. This developmental process may decrease sensitivity to sleep loss and increase the tolerance to sleep pressure, a prerequisite for adult lifestyles in modern societies.

Interaction of circadian processes and sleep homeostasis: Although sleep homeostatic and circadian processes are independent mechanisms, they interact in a complex way to control vigilance states and sleep timing. The rise of homeostatic sleep pressure during waking is opposed by the increasing circadian alertness in the course of the day, allowing adults to maintain constant levels of vigilance throughout the waking period. Conversely, during sleep, the rising circadian sleep tendency counteracts the declining homeostatic sleep pressure ensuring maintenance of sleep. The developing interaction of the two processes appears to be a key determinant for sleep-wake behavior in young humans (early infant crying behavior, adolescent sleepiness across the day). For example, a change in the phase angle of entrainment of the circadian and homeostatic processes across adolescent developoment can explain the emergence of a midday augmentation of sleep tendency even in the absence of any change in total sleep time (Figure 7). On the other hand, the development of a strong clock-dependent alerting signal in the first few months after birth may underlie the tendency for some infants to express crying behavior preferentially at certain times of day.

Summary

Biological determinants of sleep and the ways in which environment and biology interact play a major role in

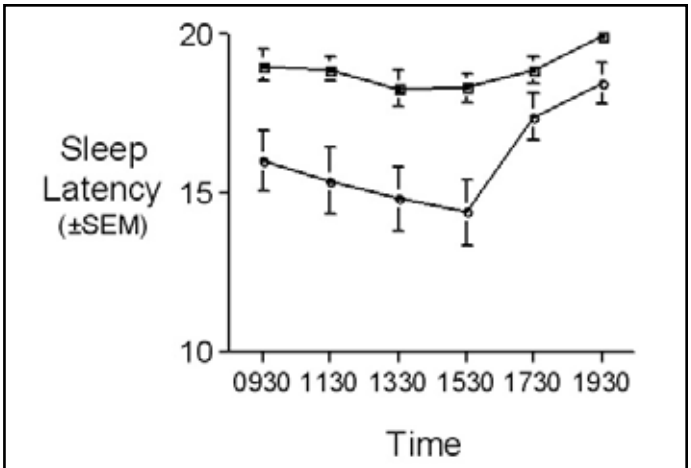

Figure 7. Sleep latency (MSLT) profile in well-slept prepubertal (square symbols) and pubertal (circular symbols) adolescents (Modified from Carskadon, M. A., Acebo, C., Jenni, O. G. Regulation of Adolescent Sleep: Implications for Behavior. Annals of the New York Academy of Sciences 2004; 1021: 276-291). © NY ACAD SCI.

establishing behavioral and developmental norms and expectations regarding normal and problematic children's sleep. While less is known about the physiological, regulatory, and genetic nature of children's sleep, we know more about the primary role of social, family and cultural systems on sleep behavior in children.

Function of sleep during development: Among the explanations for the function of sleep, two hypotheses have dominated the field: sleep is restorative for brain metabolism and sleep serves memory consolidation and learning. In view of the significant sleep need during human development, it is not surprising that a number of reseachers have proposed a major role of sleep for brain maturation, development and learning during childhood. Roffwarg and colleagues were the first to suggest that active sleep stimulates the brain in a period when external stimulation is minimal and, thus, may actively contribute to maturational processes of the central nervous system. The other sleep state, quiet sleep, may also contribute to brain development by synaptic remodeling of neurons through endogenous sources of repetitive, synchronized activity within specific neuronal intracortical and thalamocortical pathways.

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Notes