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The journey through the world of adolescent sleep

Abstract: Sleep-wake patterns and the electroencephalogram (EEG) during sleep undergo fundamental changes during adolescence. Scientific evidence indicates that these changes represent components of an extensive maturational brain remodeling process. Sleep during periods of brain maturation appears to be particularly important for health and behavior. Adolescents' sleep problems affect their cognitive and psychobehavioral functioning, making insufficient sleep during this developmental stage a significant international health concern. In this review, we summarize some key data concerning developmental changes in sleep behavior and regulation, and the association between sleep EEG changes and brain maturation. This review extends our understanding of adolescent sleep and highlights its significance for healthy development. We discuss the possibility to follow brain maturation and to detect errors in this maturational process by monitoring the developmental sleep EEG changes.

Keywords: adolescence; brain development; maturation; slow-wave activity.

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Introduction

Adolescence is a dynamic transition process from childhood to adult life. On the way to becoming adults, adolescents are challenged with self-management, individual psychosocial factors, new abilities and expectations. They pass through a rich variety of developmental stages and opportunities. The developmental transition process through adolescence is accompanied by a fundamental neurobiological reorganization that encompasses biological, psychoemotional and interpersonal changes. Neuroscientists have made outstanding advances in identifying the cognitive and behavioral correlates of this reorganization. Sleep is one aspect of behavior that changes greatly across adolescence. We review data concerning developmental changes in human sleep electroencephalogram (EEG) across adolescence and look into the world of adolescent sleep.

Pubertal development

Puberty is commonly defined as the period of physical changes by which the reproductive maturity is achieved. Puberty is characterized by the activation of the hypothalamic-pituitary-gonadal axis and gonadal maturation. Girls usually attain the ability of sexual reproduction between ages 8 and 14 years, and boys between ages 9 and 15 years (Blakemore et al., 2010). The term 'puberty' is frequently used in the same context as the term 'adolescence'. However, adolescence is the period of maturation of social and cognitive behaviors (Sisk and Foster, 2004). Gonadal maturation and behavioral maturation are closely interrelated processes, and the end point of these two processes is the mature adult with reproductive capabilities (Sisk and Foster, 2004; Blakemore et al., 2010).

The onset of puberty induces dramatic changes in hormone levels and physical growth (Sisk and Foster, 2004; Dorn, 2006). Notable among hormonal changes during puberty are remarkable increase in testosterone level for boys and in estradiol level for girls (Ducharme and Forest, 1993). Along with a gonadal maturation, the developmental process during puberty also encompasses physical and mental changes. It is suggested that the hormonal changes of puberty trigger a new burst of brain reorganization and plasticity (Sisk and Foster, 2004). However, strong evidence suggesting that puberty significantly influences some aspects of cognitive development has not yet been revealed (Blakemore et al., 2010).

Puberty is a complex process extended over years that involve various overlapping steps of biological and physical transformation (Dorn, 2006). Additionally, the timing of puberty appears to influence boys and girls in different ways (Herman-Giddens et al., 2004; Taga et al., 2006). A commonly used measure of pubertal development is Tanner staging, which assesses the approximate level of pubertal maturation based on observed body changes (Tanner, 1962).

The onset of adolescence is also a time of important changes in the psychological and social processes. During this period, teens' behavior is challenged by new abilities, insights and expectations of adult life. The developmental course of adolescence starts with the onset of puberty, which is variable, and ends with adulthood (Coleman and Coleman, 2002; Herman-Giddens et al., 2004). Puberty is strongly connected with health consequences associated with risky behaviors including substance use, accidents, and sexual behavior (Martin et al., 2002; Holm et al., 2009).

Sleep is an important aspect of adolescent development. It is widely accepted that sleep patterns change fundamentally during adolescence, and there is a growing interest in understanding whether these changes in sleep pattern are specific to age or puberty status. We will review data concerning the link between sleep EEG changes across adolescence and pubertal maturation in the following subsections.

Adolescent sleep behavior

Sleep and waking patterns exhibit substantial changes from childhood through adolescence. One of the most clearly apparent changes is the delay in the timing of sleep: adolescents have late-to-bed and late-to-rise tendency compared to younger children (Dahl and Carskadon, 1995). As early as in 1913, Lewis Terman and Adeline Hocking described a shift from 'vesperal' to 'matinal' sleep patterns in 2692 children and adolescents. They found that time in bed shows an age-related decline along with increased difficulties of morning awakenings (reviewed in Colrain and Baker, 2011). More recent research surveys of adolescent sleep behavior have shown that adolescents generally obtain significantly less sleep than younger children as a result of increasingly later bedtimes. The landmark work by Wolfson and Carskadon (1998) of 3120 Rhode Island high school students reported that 45% of 13- to 19-year-old adolescents went to bed after midnight on school nights. On weekends, the percentage of students with bedtimes later than midnight increased to 90%. According to the 2006 poll by the National Sleep Foundation, adolescents in the United States sleep less than they need. Average sleep duration on school nights was 8.4 h for 6th graders and 6.9 h for 12th graders (National Sleep Foundation, 2006). Studies in children in the USA, Canada and Brazil showed that bedtime becomes progressively later with increasing age (Andrade et al., 1993; Wolfson and Carskadon, 1998; Laberge et al., 2001). A delay in the timing of sleep during adolescence has been observed in many countries in Europe and Asia (Szymczak et al., 1993; Thorleifsdottir et al., 2002; Iglowstein et al., 2003; Tagaya et al., 2004; Yang et al., 2005; Russo et al., 2007; Chung and Cheung, 2008). Teens tend to have later bedtimes than younger adolescents even when wake-up times are controlled by school or work (Carskadon, 1982, 1990; Thorleifsdottir et al., 2002; Hagenauer et al., 2009).

Although most studies have been cross-sectional, longitudinal measures also confirm that the timing of sleep is delayed during adolescence (Andrade et al., 1993; Laberge et al., 2001). The longitudinal study by Laberge and colleagues (2001) of the developmental changes in the timing of sleep in adolescents followed from age 10 to 13 years, based on parental reports, describes results analogous to those of cross-sectional studies, mainly, bedtime delay, decline in nocturnal sleep time, and increasing differences between school and weekend sleep schedules. Actigraphy monitoring of changes in sleep timing of adolescents aged 9.9–11.2 years at the first assessment, over a 3-year period, also shows that sleep onset time is significantly delayed with advancing age (Sadeh et al., 2009).

The decline in the amount of sleep associated with the delay of the timing of sleep was initially attributed to the decline of sleep need with age. However, a longitudinal pioneering study at the Stanford University summer sleep camp examined this issue in children aged 10–16 (Carskadon, 1982). Children slept on a fixed 10-h interval from 22:00 to 08:00 h. Regardless of age or developmental stage, nocturnal sleep time stayed constant – about 9 h. These data indicated that the need for sleep does not decrease and may even increase across adolescent development (Carskadon, 1982). Several other studies have confirmed that despite the reduced amount of sleep on weekdays, the sleep need does not decrease, and adolescents tend to extend sleep on weekends and holidays (Strauch and Meier, 1988; Andrade et al., 1993; Szymczak et al., 1993). Some differences in sleep behavior among adolescents from different countries have been described, but the biological sleep need appears to be somewhat invariable regardless of the place where the children were living (O'Malley and O'Malley, 2008).

The shift to later bedtimes observed in adolescents is often reported in the context of school start times. Many adolescents have restricted amount of sleep due to an early school start time combined with a late bedtime. Evidence indicates that early school start times lead to significantly less sleep on school nights (Carskadon, 1982; Strauch and Meier, 1988; Wolfson and Carskadon, 1998, 2003; Owens et al., 2010). Analyzing sleep patterns separately on school and weekend days more comprehensively

describes developmental changes in sleep/wake behavior. Adolescents sleep longer on weekends, and weekend sleep schedules are different from their weekday schedules, possibly because of insufficient sleep on school days (Szymczak et al., 1993; Laberge et al., 2001). The average amount of weekend oversleep across ages 13–19 was found to be 1 h 50 min (Wolfson and Carskadon, 1998). About 2-h increases in weekend sleep duration were found also in other studies (Giannotti et al., 2002; Gau and Soong, 2003). The delay of sleep onset, extended sleep time and poorer sleep quality on Fridays compared to weekdays has also been reported (Sadeh et al., 2009).

Findings are inconsistent about whether there are gender differences in sleep patterns. Laberge and colleagues (2001), in a group of 10- to 13-year-olds, found that girls sleep longer on weekends compared to boys. In a survey of 3478 Japanese high school students aged 15–18 years, the mean bedtime was later and the mean sleep duration longer in the male students (Tagaya et al., 2004). However, an earlier study by Wolfson and Carskadon (1998) did not detect a sex difference in the sleep of 13- to 19-year-old adolescents.

Studies examining sleep in adolescents during school vacations, with less restricted daily schedules, also confirmed that students sleep less during the school year (Szymczak et al., 1993; Hansen et al., 2005). Late sleep-wake patterns have been reported during summer vacation compared to the school period, and the intensity of the summer delay depended on the age (Crowley et al., 2006). It has been suggested that the less restricted daily agenda for the period of vacation accounts for later sleep schedules; however parents' decreased control on teens' sleep schedules may also induce these differences (Crowley et al., 2007).

Table 1 summarizes sleep schedule alterations during adolescence observed in a number of studies from around the world. These data describe that a bedtime delay, a decline in sleep amount, and differences in weekday and weekend sleep patterns show similar trends in countries with different cultures and socioeconomic backgrounds.

Irregular sleep schedules – including discrepancies between schooldays and weekends – can contribute to a shift in sleep phase, i.e., tendency toward morningness or eveningness (Dahl and Carskadon, 1995). The shift in timing of adolescent sleep is associated with a shift in chronotype toward eveningness that typically occurs around the age of 13 years (Carskadon et al., 1993). The chronotype is predominantly defined via behavior, e.g., activity onset in animals, which strongly correlates with sleep offset (Roenneberg et al., 2004). It depends on genetic (Archer et al., 2003), environmental factors and age (Carskadon et al., 1999; Duffy and Czeisler, 2002; Roenneberg et al., 2004). Roenneberg and colleagues (2004) estimate an individual's chronotype on the basis of the sleep midpoint on days without social restrictions. They report that chronotype delays from age 10 to 20. At around age 20, a maximum of lateness in chronotype is observed. After age 20, the chronotype starts advancing again, and this change was suggested as 'the first biological marker of the end of adolescence' (Roenneberg, et al., 2004).

Behavioral factors have a major influence on sleep behavior in adolescents and contribute to their sleep delay. Indeed, the delay in timing of sleep may originate from changes in academic demands, social opportunities, part-time employment, late-evening activities, watching TV and using a computer, often without parental control of the time spent on such activities (Anders et al., 1978; Carskadon, 1990; Van den Bulck, 2004). However, because of the low variability in adolescents' sleep patterns across countries, despite broad differences in their socioeconomic backgrounds and cross-cultural variations, it has also been suggested that not only changes in psychosocial functioning but also intrinsic biological factors may induce the sleep phase delay in teens (reviewed in Carskadon et al., 2004). These biological factors are changes in both circadian and homeostatic components of sleep. Below, we provide a general background of how these processes appear to change during adolescent development.

Sleep regulation process during adolescence

Current models of sleep regulation put forward two intrinsic bioregulatory processes that determine the duration and timing of sleep-wake behavior in humans – a sleep-wake-dependent homeostatic process and a sleep-wake-independent circadian process. Carskadon et al. (2004) suggest that intrinsic changes in sleep-wake regulatory processes during adolescent development 'may be strongly related to the sleep timing and amount either as 'compelling' or 'permissive' factors'.

Changes in the circadian system during adolescence

The circadian system has a distinct anatomical substrate located in the suprachiasmatic nucleus in the anterior

Table 1 Changes in sleep-wake patterns across adolescence.

Authors	Country	Sample size	Age/grade level	Study design	Pubertal status	Results
Anders et al. (1978)	USA	218	10–13 years	Cross-sectional; sleep habits survey report	–	Trends in sleep-wake patterns across the age: – TST – decreases on school nights (by 61 min for girls, by 79 min for boys) as well as on weekends (by 20 min for both sexes) – Bedtime – delays on both school nights (by 36 min for girls and by 79 min for boys) and weekends (by 55 min for girls and by 80 min for boys)
Carskadon (1982) (subchapter: 'Normative values – nocturnal sleep')	USA	32	Group 1, 10–16 years (n=24) Group 2, 17–20 years (n=8)	Longitudinal; 3 nights of PSG conducted on a fixed 10-h interval (22:00–08:00 h) for each recording session; number of sessions varies between subjects.	Tanner staging performed in Group 1	– Sleep duration – approximately 9 h irrespective of age or maturational stage – Sleep structure – slow-wave sleep (stages 3 and 4) tends to decline and sleep stage 2 tends to increase across the second decade. The apparent plateau of these changes is observed in Tanner stage 5 and in older adolescents (group 2)
Carskadon (1982) (subchapter: 'Surveys of sleep habits')	USA	218	10–13 years	Cross-sectional; sleep habits questionnaire	–	– The tendency to go to bed later and arise later on non-school nights compared to school nights, with greater differences at older ages – TST in the 10 year olds – identical on school and non-school nights (587 min) – TST in the 13 year olds – a significant difference between school nights (522 min) and non-school nights (562 min)
Strauch and Meier (1988)	Germany	190	10–14 years at the study initiation in 1975	Longitudinal; 10 year period with surveys at 2-year intervals; questionnaire-based study	–	– TIB on weekdays – decreases from an average of 9.9 h (in 1975, n=190) to 7.7 h (in 1983, n=137) – TIB on weekends and during vacation – shows similar trends but less pronounced (1.1 h on weekends; 1.6 h on vacation) – Wish for more sleep – every second adolescent in each survey
Andrade et al. (1993)	Brazil	66	12–16 years	Longitudinal; 3 time points at 6-month intervals (semesters); questionnaires based study	Tanner staging performed	– Sleep schedule changes – sleep onset occurs about 1.0 h later, wake-up time about 3.0 h later, and sleep length is 1.0–1.5 h longer on weekends compared to weekdays at all time points – Weekend oversleep – an increase from 1 h 18 min at first semester to 1 h 50 min at the third – Sleep onset per semesters – no delay
Carskadon et al. (1993)	USA	458	11–12 years (6th grade)	Cross-sectional; questionnaire-based study	Pubertal status evaluation with self-rating questionnaire	– Bedtime and pubertal status – weekday bedtime is significantly related to puberty stage: students with higher puberty scores report later bedtimes – M/E status – significant correlation with pubertal status in girls; only trend in boys; nonsignificant relation with psychosocial factors examined (school environment and birth order)

(**Table 1** Continued)

Authors	Country	Sample size	Age/grade level	Study design	Pubertal status	Results
Szymczak et al. (1993)	Poland	64	10 years, 40 subjects 14 years, 24 subjects	Longitudinal; sleep diaries	–	– The mean sleep duration – 10.2 h (10 year olds) and 8.7 h (14-year-olds) during the school nights – Sleep duration on weekends – younger subjects sleep longer; a similar tendency is present in the older group – Sleep duration during vacations – increases considerably compared to the school year, without weekly variations in sleep length
Wolfson and Carskadon (1998)	USA	3120	13–19 years	Cross-sectional; sleep habits survey report	–	Trends in sleep-wake patterns across age groups (13–14; 15; 16; 17–19 years): – School nights – TST decreases by about 40 min; bedtime delays by about 45 min – Weekend nights – TST decreases by about 50 min; bedtime delays by about 60 min
Laberge et al. (2001)	Canada	1146	10–13 years	Longitudinal; questionnaire-based study	Pubertal status evaluation at age 13 with Pubertal Development Scale	Age trends in sleep-wake variables: – School nights – TIB decreases approximately by 63 min; bedtime delays by 61 min – Weekend nights – TIB decreases only by 14 min over a 3-year period; bedtime delays by 69 min – Sleep and pubertal status – subjects with higher pubertal status sleep longer on weekends and have greater weekend oversleep than subjects with lower pubertal status
Thorleifsdottir et al. (2002)	Iceland	688	1–20 years	A cross-sectional as well as a longitudinal approach – a 10-year period with surveys at 5-year intervals; sleep diary, questionnaires	–	– Sleep schedule changes – a shift of the bedtime to later hours with increasing age – Sleep duration – decreases on weekdays across a 10-year period in children up to 15 years old. At the age of 9, total sleep becomes significantly longer on weekends (15±47 min) than on weekdays, with the greatest difference at the age of 13 (64±69 min)
Gau and Soong (2003)	Taiwan	1547	10–14 years (4th–8th grades)	Cross-sectional; questionnaire-based survey	Pubertal status evaluation by Pubertal Development Scale	– The sleep-phase preference across grades – M/E score decreases and the proportion of evening-type subjects increases across school grades. The grade level is a more important factor contributing the sleep-phase preference transition than age or pubertal development – M/E and sleep schedule – the evening group students go to bed later and get up later, tend to sleep less, and have greater differences between school days and weekends in terms of bedtime, rise time and nocturnal sleep duration than morning types

(**Table 1** Continued)

Authors	Country	Sample size	Age/grade level	Study design	Pubertal status	Results
Iglowstein et al. (2003)	Switzerland	493	1 month–16 years	Longitudinal; structured interviews with the parents	–	– Reference value for age 8–16 years – duration of nighttime sleep decreases from an average of 10.4 h at age 8 to an average of 7.9 h at 16 years of age – A cohort effect – comparison of 3 birth cohorts (1974, 1979 and 1986) reveals a delay in the bedtime across cohorts while wake time remains unchanged. A decreasing trend in the bedtime with increasing age is apparent in each cohort
Tagaya et al. (2004)	Japan	3478	15–18 years (1st–3rd grades)	Cross-sectional; questionnaire-based survey	–	– Sleep and grade level – the mean bedtimes delays and sleep duration decreases as the grade level goes up – The average sleep duration – 380 min – Gender effect – the female students sleep less than male students
NSF poll 2006	USA	1602	11–17 years (6th–12th grades)	Cross-sectional; survey/ telephone interviews	–	Trends in sleep-wake patterns across the grades: – Average TST – decreases from 8.4 to 6.9 h on school nights and from 9.2 to 8.4 h on weekends – Bedtime delay – by 98 min on school nights, and by 134 min on weekend nights
Yang et al. (2005)	Korea	1457	5th–12th grades; mean age 13.7±2.4 years	Cross-sectional; school sleep habits survey	–	Trends in sleep-wake patterns across four grade categories (5th/6th–11th/12th): – School nights – average bedtime delays by about 130 min; TST decreases by more than 170 min – Weekend nights – average bedtime delays by about 45 min, and average TST is 36 min shorter. In the higher grades the magnitude of weekend oversleep increases
Russo et al. (2007)	Italy	1074	8–14 years	Cross-sectional; school sleep habits survey	–	Trends in sleep-wake variables across age (seven levels: 8, 9, 10, 11, 12, 13, 14 years): – School nights – average sleep duration decreases by 65 min. bedtime delays by 53 min. The rise time remains relatively stable – Weekend nights – sleep duration decreases by 4 min, bedtime delays by 65 min. The rise time shows a significant increasing linear trend
Chung and Cheung (2008)	Hong Kong	1629	12–19 years	Cross-sectional survey; questionnaire-based survey	–	– Average bedtime – delays by 64 min on weekends compared to school nights. Bedtime across age groups (12–13; 14; 15; 16; 17–19 years) – delays by 47 min on school nights, by 43 min on weekends – Average rise time – delays by 195 min on weekends compared to school nights; rise time across age groups – remains constant on school nights, delays by 36 min on weekend nights – Average weekend oversleep – 131 min. Weekend oversleep increases by 59 min across age groups

(**Table 1** Continued)

Authors	Country	Sample size	Age/grade level	Study design	Pubertal status	Results
Sadeh et al. (2009)	Israel	94	9.9–11.2 years (at 1st assessment)	Longitudinal; actigraphy assessment for 2 successive years (three time points)	Pubertal status evaluation by Pubertal Development Scale and Sexual Maturation Scale	– Sleep onset – delays by an average of 50 min across 2 years of development (from time 1 to time 3) – True sleep time (sleep time without periods of wakefulness) – decreases significantly by an average of 37 min – On Fridays, sleep onset delays and true sleep time increases compared to school days – Sleep and puberty measures – significant correlations are detected, particularly during the early stage of the study

TST, total sleep time; TIB, time in bed; M/E, morningness/eveningness.

hypothalamus. The suprachiasmatic nucleus, the master biological clock, regulates the timing of mammalian sleep/wake cycle and most circadian (24 h) behavioral, physiologic and biochemical rhythms. Light is the primary synchronizing stimulus for the circadian system (Czeisler et al., 1981). The circadian system is especially sensitive to light during the night – the usual sleep period in humans.

Three mechanisms have been proposed to define how sleep phase delay may originate from developmental changes in the circadian timing system (Jenni and Carskadon, 2005).

First, *circadian phase is delayed in association with puberty*. Studies have shown that several distinct changes of the circadian process that influence the adolescent sleep phase delay may occur during puberty. The first effort to examine developmental changes in the circadian timing system during adolescent development was performed in a landmark study by Carskadon and colleagues in 1993. In this survey of 275 sixth-grade girls and 183 sixth-grade boys, the puberty score was significantly associated with circadian phase preference score in girls; a similar but non-significant trend was found in boys. Physically mature adolescents also reported more 'evening'-type circadian preference even for the same grade level of school (Carskadon et al., 1993). Although the measures were indirect and self-reported, these data provided the first evidence for the implication of biological processes in the delay of adolescent sleep timing. Subsequent studies used more precise measures, for example, melatonin secretion that is regulated by the circadian timing system. Carskadon et al. (1997) found that the pubertal stage measured by physicians correlated with the offset phase of melatonin secretion so that more mature children showed a later phase of the melatonin offset. Salti et al. (2000) reported that melatonin concentration, quantified in eight girls and eight boys between 19:00 and 07:00 h was affected by pubertal rather than chronological age. In addition, salivary melatonin secretion onset was about 1 h earlier in the prepubertal (Tanner stage 1) subjects than in mature (Tanner stage 5) adolescents (Taylor et al., 2005). Acebo and colleagues (2003) showed that Tanner stage was the only significant predictor of melatonin level and amplitude in a linear regression analyses with the following variables: age, body mass index, circadian phase preference and Tanner stage. Similar results were reported by Crowley and colleagues (2012). Furthermore, Crowley et al.'s study pointed out that melatonin amplitude measures decline with advancing Tanner stage in a similar manner in boys and girls.

These studies provide some evidence to suggest that the delay of circadian timing is associated with puberty.

Moreover, a review of the studies examining the daily rhythms of mammals during pubertal development strongly supports the hypothesis that a delay in circadian phase at the time of puberty is a common observable fact across mammalian species (Weinert and Waterhouse, 1999; Golub et al., 2002).

Second, *the lengthening of the intrinsic period of the circadian clock during puberty may account for the delay of the circadian phase*. Assessment of circadian period has become feasible using forced desynchrony. Under this technique, the circadian timing system runs free from the normal 24-h entrainment cues, and the intrinsic period of the rhythm can be assessed through the timing of the daily phase markers (Dijk and Czeisler, 1995). A 28-h forced desynchrony protocol was imposed on 10 healthy adolescents in a study by Carskadon et al. (1999). Analyses of the intrinsic period showed that the circadian period appeared longer than 24 h. There was no correlation of circadian period with pubertal status in this small sample. A later forced desynchrony study of 27 adolescents also did not find evidence of pubertal changes in the circadian period (Carskadon and Acebo, 2005). Although not associated with puberty, the mean period of the circadian clock in these adolescents (24.27 h) was significantly longer than in adult samples (24.12 h) recorded in a similar 28-h forced desynchrony paradigm (Czeisler et al., 1999). Although the data at this time are not conclusive, they are suggestive of a longer internal period in adolescents. Longitudinal studies with more subjects involved are essential to confirm the changes in intrinsic circadian period across adolescent development.

Third, *sleep phase delay may be associated with increased sensitivity to evening light or decreased sensitivity to morning light during pubertal development*. Findings provide only suggestive support for this hypothesis (Carskadon et al., 2004). The tendency of the phase delay in adolescents may also be strengthened by the changes in the time of light exposure (e.g., by TV watching or computer use in the late evening) that may influence the circadian timing system via phase resetting mechanism (Jenni and Carskadon, 2005; Crowley et al., 2007; Hagenauer et al., 2009). Additional research is needed to clarify circadian system response to light across adolescent development.

In summary, current evidence indicates that in addition to the behavioral factors, distinct changes of the circadian timing system during puberty may drive the delay in the timing of sleep in adolescents. Table 2 summarizes some key findings from studies on circadian parameters and pubertal maturation.

Changes in the homeostatic system during adolescence

Delta EEG power in adolescents

Delta waves, also referred to as slow waves in the sleep EEG, are a major electrophysiological characteristic of non-rapid eye movement (NREM) sleep. Numerous studies have demonstrated that NREM delta EEG power, a spectral analysis measure of NREM delta EEG activity, is determined by prior waking duration and shows marked decline across NREM periods (NREMPs) (Webb and Agnew, 1971; Feinberg, 1974; Feinberg et al., 1980; Borbely, 1982; Dijk et al., 1989). According to the homeostatic model of sleep (Feinberg, 1974; Borbely, 1982), NREM delta EEG power is a correlate of a homeostatic process and changes in its intensity serve as an indicator of sleep homeostasis.

The homeostatic properties of NREM delta EEG can be summarized as follows: First, the longer the time spent awake, the higher the delta power in the subsequent sleep that decreases across the night (Feinberg, 1974; Borbely, 1982; Tononi and Cirelli, 2006). Second, delta is conserved, i.e., delta power occurring in daytime naps reduces delta in post-nap sleep (Campbell and Feinberg, 2005). Delta EEG activity, an indicator of sleep depth, is strongly related to age – it reaches a peak in childhood, declines steeply across adolescence and then continues to decline slowly but still remarkably across adulthood (Feinberg and Carlson, 1968; Ehlers and Kupfer, 1989; Feinberg et al., 1990a). Computer EEG analysis has demonstrated that NREM theta EEG (EEG activity in the theta frequency range) also displays homeostatic (Borbely et al., 1981; Campbell et al., 2011) and age-dependent properties (Gaudreau et al., 2001; Jenni and Carskadon, 2004; Campbell et al., 2011) resembling those of delta.

Longitudinal measurements are enhancing our knowledge of adolescent sleep EEG changes. The recent multiyear longitudinal study of sleep EEG in two adolescent cohorts, one studied beginning at age 9 and the other at age 12, investigated age trajectories of sleep EEG changes from childhood through late adolescence. This study by Feinberg, Campbell and colleagues is the most extensive longitudinal study of adolescent sleep carried out so far (Campbell and Feinberg, 2009; Feinberg and Campbell, 2010; Campbell et al., 2011). Their longitudinal data revealed information about the patterns of NREM delta (1–4 Hz) and theta (4–8 Hz) EEG maturation that were not detected by previous cross-sectional research. Between ages 9 and 18 years, delta EEG power as well as theta EEG power (a spectral analysis measure of EEG activity in the theta frequency range) declined steeply and significantly. For both delta

Table 2 Circadian parameters and pubertal maturation.

Authors	Sample size	Age	Study design	Pubertal status	Results
Carskadon et al. (1997)	19 (9 girls, 10 boys)	11.2–14.4 years	CR	Tanner stages 1–4	– The offset phase of melatonin secretion is significantly correlated with age and Tanner stage – A trend for a positive correlation with Tanner stage is present for midpoint phase of melatonin secretion
Carskadon et al. (1999)	10 (5 girls, 5 boys)	10.9–15.2 years	FD	Tanner stages 2–5	Average intrinsic circadian period for: – Core temperature is 24.3 h (SD ±0.2) – DLMO is 24.33 h (SD ±0.21) – Dim-light melatonin offset is 24.35 h (SD ±0.21)
Salti et al. (2000)	16 (8 girls, 8 boys)	8.7–16.8 years	12 h (19–7 h) blood sampling at 30-min intervals	Tanner stages 1–4	– Negative relationship of 12-h melatonin AUC is seen more prominently vs. pubertal stage than vs. chronological age (in boys and girls) – Ultradian changes with periods of 3.4 and 1.5 h, putatively associated with rapid eye movement sleep cycles, characterize nocturnal melatonin in boys and girls
Taylor et al. (2005)	20 (12 girls, 8 boys)	Prepubertal group: mean age 11.1 years (SD ±1.3) Pubertally mature group: mean age 13.9 years (SD ±1.2)	CR	Prepubertal group: Tanner 1 Pubertally mature group: Tanner 5	– DLMO is earlier in the Tanner 1 group (mean clock time 20 h 33 min, SD 49 min)than in the Tanner 5 group (mean clock time 21 h 29 min, SD 42 min) – Sleep tendency after 14.5, 16.5 and 18.5 h awake is lower in Tanner 5 group than in Tanner 1 group (after controlling for circadian phase)
Carskadon and Acebo, 2005	27 (14 girls, 13 boys)	9–15 years	FD	Tanner stages 1–5	– Average intrinsic circadian period for DLMO in whole sample is 24.27 h (SD not reported) – Nonsignificant trend is found for the length of average intrinsic circadian period when comparing Tanner 1 (24.21 h, SD ±0.2) and Tanner 5 groups (24.27 h, SD ±0.18)
Crowley et al. (2012)	69 (30 girls, 39 boys)	9.6–17.8 years	CR	Tanner stages 1–5	– Melatonin amplitude measures (AUC) decline with advancing Tanner stage (in boys and girls) – The girls secrete more melatonin compared to boys – Tanner stage and sex explain AUC variability (but age and BMI do not)

CR, constant routine condition; FD, forced desynchrony condition; DLMO, salivary dim-light melatonin onset; AUC, area under the curve; BMI, body mass index.

and theta EEG, average spectral power for the two cohorts was similar between ages 12 and 15 years, where the cohort ages overlap. For this period, the age-related decline did not differ between cohorts (Campbell et al., 2011). The longitudinal time course of delta EEG maturation, one of the major findings of this study, is described as follows: It is initiated between ages 11 and 12, delta power decline is remarkably steep thereafter, and its rate of decline appears to slow by age 17 (Campbell and Feinberg, 2009; Feinberg and Campbell, 2010; Campbell et al., 2011).

Kinetics of NREM delta EEG power in adolescents

The dynamics of the NREM delta EEG power across night represents a powerful tool to study the kinetics of sleep homeostasis. The two-process model of sleep regulation (Borbely, 1982) postulates that the homeostatic process, or process S, increases exponentially during wakefulness and decreases as an exponential function during sleep. Many studies have been devoted to the study of the kinetics of NREM delta EEG power across adolescents. In a study of sleep EEG in young adults and elderly subjects, Feinberg and Campbell (2003) found that normalized 0.3–3 Hz power density increased linearly across daytime naps and declined linearly across NREMPs with similar slopes of accumulation and decline for young and elderly subjects. It was therefore predicted that the delta power decline across NREMPs in adolescents would also be linear with a slope similar to that found in the two older groups (Darchia et al., 2007). This assumption contradicted the earlier report by Gaudreau et al. (2001) that normalized delta across the night declines more steeply in children and adolescents (mean age 7 and 15 years) than in young (24 years) and middle-aged (45 years) subjects.

Later on, a study from Feinberg's group (Darchia et al., 2007) found the explanation for these discrepancies. This study showed that different designations of delta band (0.75–4 Hz for Gaudreau et al., 2001, and 0.3–3 Hz for Feinberg and Campbell, 2003) yielded different trends across NREMPs due to unusual pattern of the decline in very low frequencies (VLF) <1 Hz EEG. VLF power exhibits approximately equal power in the first two NREMPs and then declines (Achermann and Borbely, 1997; Campbell et al., 2006). Darchia et al. (2007) have demonstrated that the normalized delta power decline across NREMPs in adolescents (mean age 10.8 years) show concave curvilinear decline even when the VLF component is included in delta band boundaries.

NREM delta EEG power trends across the night reflect the progression of a recuperative process of sleep (Feinberg and Campbell, 2003). Delta power decline across the night in adolescents is significantly steeper than in young adults (Gaudreau et al., 2001; Darchia et al., 2007). Even when standardized as a percent of the all-night mean, delta power declines more steeply across NREMPs in adolescents, primarily due to a disproportionately high value in the first NREMP (NREMP1). When NREMP1 is excluded from the analyses, the decline in normalized delta power (for any delta-band designation) across NREMPs do not vary significantly between the different age groups (Darchia et al., 2007).

In summary, the decline of normalized delta power across the night shows different trends at different ages. The steeper normalized delta power decline in adolescents indicates that the rate of homeostatic recuperation is higher in this age group, and this intense recuperation is accomplished more rapidly and mainly in the NREMP1.

Sleep homeostatic regulation during adolescence

As already noted, the sleep-wake homeostatic process or process S reflects the homeostatic sleep pressure (the drive to fall asleep), which accumulates during wakefulness and dissipates during sleep (Feinberg, 1974; Borbely, 1982; Daan et al., 1984). Slow-wave activity (SWA), defined as EEG power in the low-frequency range (0.75–4.5 Hz), has been used as a physiological marker to model the process S. Several studies were published in recent years on pubertal changes in the sleep EEG within the context of the homeostatic model. Although it has been described that delta power decreases substantially across adolescence, it was not clear whether this decline reflects developmental changes of the brain structures or changes in the homeostatic process of sleep. Jenni and Carskadon (2004) and Jenni et al. (2005a,b) investigated this issue with cross-sectional data. They found that across-night decline in SWA did not differ significantly across pubertal development in any of process S parameters. However, the build-up of the homeostatic sleep pressure during waking in prepubertal or early pubertal children (mean ages 11.9 years, n=7) was faster compared to that in mature (mean age 14.2 years, n=6) adolescents (Jenni et al., 2005a). In addition, delta EEG response to sleep deprivation was stronger in older adolescents. It has been suggested that sleep homeostasis exhibits specific maturational changes during puberty: At younger ages, the slow-wave generation capacity is reached with less waking, and consequently, at the end

of the day young children are closer to their maximum capacity for delta wave generation, whereas slow accumulation of sleep homeostatic pressure in mature adolescents enables them to stay awake longer (Jenni et al., 2005a). It has been proposed that mature adolescents may have a higher tolerance to prolonged wakefulness that facilitates their transition to adult lifestyles and to meet modern societies' common demand – functioning under sleep deficits (Jenni and O'Connor, 2005; Jenni et al., 2005a). Furthermore, the same group of researchers described that sleep pressure during extended waking (14.5, 16.5 and 18.5 h) was higher near bedtime in prepubertal than in mature adolescents. These findings supported the authors' hypothesis that developmental changes of intrinsic sleep-wake regulation process may physiologically mediate sleep phase delay in adolescents (Taylor et al., 2005).

Recent longitudinal data further clarify the regulation of delta and theta EEG across NREMPs (Campbell et al., 2011). It was found that delta energy [total delta power in artifact-free EEG ($\mu V^2 \cdot s$)] in the NREMP1, standardized as a percent of the total delta power in five NREMPs, is higher at younger ages and declines across adolescence. Thus, the homeostatic sleep need that accumulates faster during wakefulness in younger adolescents also dissipates more rapidly during sleep, as is apparent in the NREMP1. In addition, maturational change in the homeostatic regulation of sleep within the night was reflected by the age-related decline in SWA at the start of the night, SWA_0 (delta power at time 0). Such decline further indicates that the recuperative processes reflected by the 1–4 Hz EEG are more concentrated in the first part of the night at younger ages. Despite the fact that Tau (the time constant of the decline) for delta did not show age-related changes, the SWA_0 decrease indicates a reduction in the rate of across-NREMP decline of normalized delta because the delta decline is initiated at a lower level but falls to a similar or higher asymptote (Feinberg and Campbell, 2010; Campbell et al., 2011).

Even stronger age-related changes were found for the homeostatic regulation of theta. Compared to delta, the decline in the standardized value of theta energy [total theta power in artifact-free EEG ($\mu V^2 \cdot s$)] in the NREMP1 was slightly larger, and the yearly decline of the theta production at the start of the night, TWA_0 (theta power at time 0) exceeded the yearly decline in SWA_0 (Campbell et al., 2011). These age changes in the two main homeostatic frequency bands reflect maturational changes in homeostatic sleep regulation. It has been proposed that these changes are signs of the pervasive adolescent brain reorganization driven by synaptic pruning (Feinberg, 1982).

In summary, longitudinal data provide strong evidence to discuss slow-wave sleep homeostasis in the context of brain development. Children accumulate homeostatic sleep need more rapidly; consequently, the rate of recuperation at the start of sleep at night is high. Accumulation of the homeostatic sleep need becomes slower as children mature. The slow accumulation positions adolescents lower on the recuperation curve that is reflected in the decline of the proportion of delta power in NREMP1 and in the decline in SWA_0 (Feinberg and Campbell, 2010; Campbell et al., 2011).

NREM delta decline and pubertal maturation

The establishment of reproductive capability and the decline of delta sleep EEG during adolescence represent basic signs of brain maturation (Feinberg et al., 2011). A number of studies have been devoted to the examination of the possible causal relationship between these two processes. Carskadon et al. (1980) investigated this point in an early longitudinal study and found a significant correlation between delta decline and pubertal maturation. They also reported that this relation was independent of age. More recent work from the same group again reported the strong correlation of the NREM delta decline with the increase of Tanner stages (Jenni and Carskadon, 2004; Jenni et al., 2005a).

Data from the multiyear longitudinal study by Feinberg and colleagues gives a strong background to examine the relationship of delta decline to pubertal maturation. In an early publication of these data, it was reported that the timing of delta power decline across adolescence show sex differences (Campbell et al., 2005). In brief, after 1 year of longitudinal study, it was revealed that NREM delta EEG power begins to decline earlier in girls than in boys. It was suggested that sex differences in delta power density may be related to earlier synaptic pruning in girls (Campbell et al., 2005). Sex differences in delta power decline were confirmed after four semiannual recordings (Feinberg et al., 2006). Data again suggested an earlier delta decline in girls than in boys, but the slopes of decline did not differ. This result is consistent with the earlier decline in frontal gray matter thickness in girls reported in magnetic resonance imaging (MRI) studies (Giedd et al., 1999). In addition, a strong relation between the rate of delta decline and the rate of pubertal maturation measured by Tanner staging has been reported in the publication by Feinberg and colleagues (2006). However, with the age

effect statistically controlled, the relation between delta decline and Tanner staging was no longer significant. Additional data from the same subjects (Campbell et al., 2012) showed that although the rate of the delta decline was not associated with the rate of pubertal maturation, the timing of both maturational processes was related – a highly significant relation between the age of most rapid pubertal maturation and the age of most rapid delta decline has been observed. It was also demonstrated that this timing relationship was independent of sex differences, i.e., the earlier delta power decline in girls compared to boys (Campbell et al., 2012). The authors suggest that the timing of cortical synaptic pruning, considered as the most possible cause of delta decline, is strongly related to the timing of puberty. Additionally, it has been found that NREM theta maturation also illustrates a significant association with the timing of pubertal maturation. Thus, findings of this study further support a link between pubertal maturation and brain development.

In summary, scientific evidence clearly indicates that the timing of the adolescent brain maturation represented by the decline in delta EEG is significantly linked to the timing of pubertal maturation. However, further investigation is needed to clarify the casualty or independence of those processes.

Link between brain maturation and sleep EEG changes

Brain development is an area of research that has received increasing interest in recent years. Development of mammalian central nervous system requires formation and stabilization of synaptic connections and neuronal circuits and the accuracy in these processes is essential to function properly.

The human brain undergoes significant changes in the brain structure and neuronal connectivity during the transition from childhood to adulthood. It has been shown that in humans as well as in rhesus monkeys, cats and mice, development of the cerebral cortex is characterized by an initial overproduction and redundancy in synaptic connections followed by neuronal or synaptic pruning through pre-adult years (reviewed in Rakic et al., 1994). The process of synaptic pruning is thought to be necessary for the refinement of brain connectivity. Histological studies of postmortem brain tissue provided the evidence for the decline in synaptic connectivity across adolescence (Huttenlocher, 1979; Huttenlocher and Dabholkar, 1997). It has been found that synaptic density in humans increases steeply in the first years of life, reaching a peak in childhood. Thereafter, synaptic density declines across adolescence by about 50% to reach the adult value.

The most well established sleep EEG change from childhood through adolescence is a steep decline in NREM delta EEG activity (Coble et al., 1987; Feinberg et al., 1990a). The synaptic pruning hypothesis has been advanced as a possible explanation for this developmental decline (Feinberg, 1982; Feinberg et al., 1990a,b; Tarokh and Carskadon, 2010). Changes in delta EEG activity are measured by changes in delta spectral power. Although the relationship between delta power and the reduction of the number of cortical synapses has not been directly examined, there are two ways by which synaptic pruning may reduce slow-wave EEG activity. Synaptic pruning may decrease slow-wave amplitude not only by diminishing the number of synchronously oscillating neurons but also by decreasing the requirement for recuperation provided by NREM sleep. More specifically, loss of connectivity between neurons would decrease the intensity of waking brain activity that would result in decrease of recuperative need (Feinberg and Campbell, 2010). This view has been emphasized in recent papers describing that the sleep SWA is a reliable indicator of net changes in synaptic density/strength because neuronal synchronization depends on the number or the strength of cortical synapses or both (Esser et al., 2007; Vyazovskiy et al., 2009; Kurth et al., 2010a; Ringli and Huber, 2011). It is now becoming recognized that the need for the sleep-dependent recuperation is a function of the intensity of waking neuronal activity as well as of the waking duration (Feinberg, 1982; Tononi and Cirelli, 2006).

Maturational brain changes across adolescence could also be described by changes in the brain metabolic rate. Changes in the brain metabolic rate – the straight measure of the intensity of brain activity during wakefulness – show interesting parallels to neuronal pruning. Positron emission tomography studies (Chugani et al., 1987) have demonstrated that waking brain metabolic rate rises rapidly in infancy, remains high in childhood, and drops by about 50% across adolescence. Later on, it has been noted that all three important indices of brain development – synaptic density, brain metabolic rate, and NREM delta EEG activity – fit the trajectories of a gamma distribution model (a common statistical probability distribution). As seen in Figure 1, the decline of synaptic density and waking cerebral metabolic rate parallels with the decline in delta wave amplitude across adolescence, suggesting that these processes may represent biologically related components of brain development (Feinberg et al., 1990b).

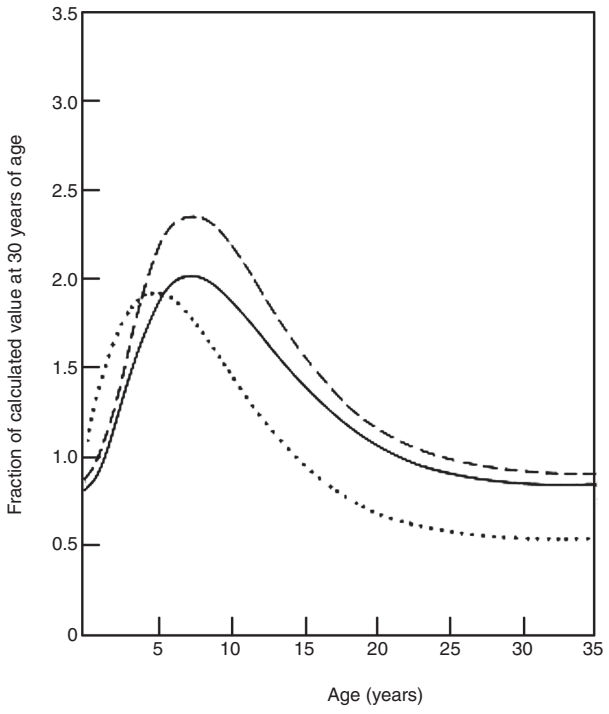

Figure 1 A gamma distribution model describes maturational curves for synaptic density squared (dots), delta wave amplitude (dashes) and cortical metabolic rate (solid line).
Data were standardized to the value at 30 years of age for each measure. Reprinted with permission from Elsevier (Feinberg et al., 1990b).

One of the important anatomical markers of adolescent brain maturation is change in gray matter volume that can be tracked *in vivo* with MRI. A number of MRI studies have reported the gray matter volume increase in childhood; the growth process is followed by a rapid decline in adolescence and by a more gradual decline thereafter (Jernigan et al., 1991; Giedd et al., 1999; Giedd, 2004; Gogtay et al., 2004; Whitford et al., 2007). Thus, the developmental time course of changes in gray matter volume has a pattern similar to what has been seen for slow-wave EEG. The regional differences in the developmental variations both for gray matter and for EEG will be discussed further. As regards white matter, studies have reported increases in its volume between childhood and adolescence (Benes et al., 1994, Whitford et al., 2007). White matter gain reflects increased axonal myelination throughout adolescence (Paus et al., 2001) and is associated with the development of language and memory skills (Nagy et al., 2004).

There are only few studies that have investigated concurrent changes in gray matter volume and EEG indexes as a function of age by applying both MRI and EEG techniques to healthy subjects. Whitford and colleagues (2007) have examined anatomical and neurophysiological brain changes in adolescence and early adulthood and found evidence for significant structural brain changes in terms of gray matter decrease in the frontal and parietal cortices. They also found that EEG activity, especially in the slow-wave band, shows a decreasing pattern similar to the reduction in gray matter volume in corresponding cortical regions. The authors suggest that gray matter reduction is related to the elimination of synapses, which would result in an observed decrease in EEG power. A recent study by Buchman et al. (2011) also observed age-related changes in cortical gray matter, confirming other reports (Gogtay et al., 2004; Sowell et al., 2004). They also examined the relationship between gray matter and sleep EEG. The authors found that the reductions in sleep SWA and gray matter volume/thickness are correlated. The highest correlation was observed for the same areas that show the largest decrease in gray matter during childhood and adolescence, supporting the view that SWA could be a marker of maturation of cortical neuronal networks (Buchman et al., 2011). Thus, both studies have observed the developmental decline of EEG power that mirrored the reduction in cortical gray matter. Furthermore, the EEG power decline and its positive correlation with gray matter was not limited to SWA range and was apparent for other EEG frequencies (to a lesser extent), indicating that EEG most possibly reflects a global process of cortical maturation.

In summary, the observation that age-related changes in SWA show the same maturational pattern as the metabolic and synaptic changes stimulated a research for other evidence of the relationship between sleep and brain development. Such evidence comes from MRI studies on gray matter-EEG relationship and suggests that EEG measures might be considered as the best noninvasive tool to track adolescent brain maturation.

Topographic changes in adolescent sleep EEG maturation

Studies published on the maturational changes of NREM EEG homeostatic frequencies across adolescence generally report data from a single C3 or C4 derivation. Data from other derivations are limited. To investigate topographical differences in adolescents' sleep EEG spectral characteristics, Jenni et al. (2005b) recorded sleep EEG from anterior (Fz/Cz) and posterior (Pz/Oz) bipolar derivations in two age groups: 20 early adolescents (Tanner 1/2) and 20 mature adolescents (Tanner 4/5). They found that sleep

EEG spectral characteristics in adolescents show state- and frequency-dependent regional differences that are similar in both developmental groups. Jenni et al. (2005b) also found that the rate of the decline of the sleep homeostatic process across the night is independent of derivations or developmental groups, supporting their earlier finding that the nocturnal dynamics of the homeostatic sleep pressure is constant across pubertal development (Jenni and Carskadon, 2004; Jenni et al., 2005a). As regards regional distribution of sleep EEG in NREM sleep, an anterior predominance was present for over almost the entire frequency range in a group of early adolescents. In mature adolescents, the anterior predominance was limited to the delta and sigma ranges (Jenni et al., 2005b), similar to that in adult subjects (Landolt and Borbely, 2001; Massimini et al., 2004). In REM sleep, a frequency predominance for posterior (low delta, alpha, and sigma ranges) as well as for anterior (theta and beta ranges) regions were remarkably similar in both developmental groups (Jenni et al., 2005b).

NREM EEG topography has been examined in longitudinal studies as well. A short-term longitudinal study by Tarokh and Carskadon (2010) showed that sleep EEG power in delta/theta bands declines from initial (9–10 years) to follow-up session (1–3 years later) in all derivations (two central, two occipital), but the decline is largest for the left central (C3) and right occipital (O2) EEG. These findings, although derived from a small sample size, suggest the hemispheric differences in adolescent EEG maturation.

A long-term longitudinal study from Feinberg et al. (2011) compared longitudinal age trajectories of NREM delta and theta EEG across 9 years of adolescence, recorded from anterior, central and occipital areas (Feinberg et al., 2011). The authors report that the overall trajectories of the delta power decline across adolescence are similar at the frontal, central and occipital electrode sites (Figure 2). However, it has been found that despite similar trajectories, the timing of delta EEG maturation shows topographic differences – the delta decline starts earliest at O1 and latest at Fz. The decline of delta power at right and left central leads (C3 and C4) was nearly identical. Thus, data regarding the hemispheric asymmetry in the delta power decline at central leads are conflicting and require further investigation (Feinberg et al., 2011). The early decline of delta EEG in the occipital region is also consistent with a recent report by Baker et al. (2012). They have explored longitudinal changes of adolescent (11–14 years) power spectrum in NREM and REM sleep and found that the occipital derivation shows greater decline than central and frontal derivations.

The maturational pattern of theta EEG power exhibits regional differences to a lesser extent than delta power,

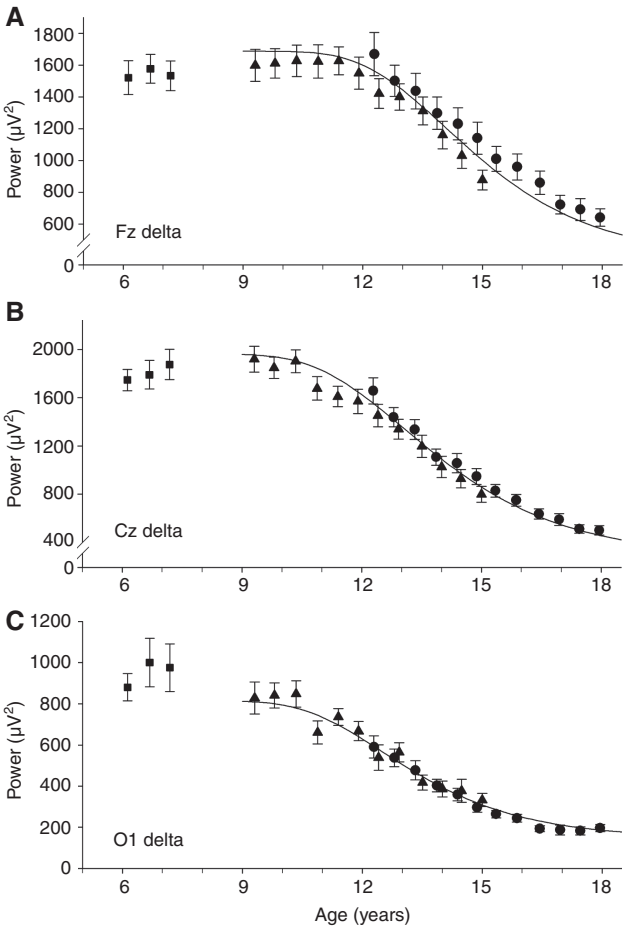

Figure 2 Average (±SE) delta power at each semiannual recording plotted against age for Fz (A), Cz (B) and O1 (C).
A Gompertz function calculated with SAS nonlinear mixed effect analysis is fit to the data from the C9 (triangles) and C12 (circles) cohorts. Data from the C6 (squares) cohort are shown but were not used to generate the function. In all three derivations, delta power declined steeply across adolescence but the magnitude and timing differed between sites. The decline began earliest at the O1 electrode and latest at the Fz electrode. The curves for the C9 and C12 cohorts showed excellent agreement in the ages of overlap (12–15 years). Reproduced from Feinberg et al. (2011).

as reported in the above-mentioned longitudinal study (Feinberg et al., 2011). Specifically, theta power declines earlier than delta power but without the back-to-front maturational pattern found for delta. However, site differences in the magnitude of theta power decline have been detected. Theta EEG manifests a shift in the ratio of Fz/Cz power resembling that of delta EEG, but much smaller. The increase in the Fz/Cz power ratio across adolescence is 14% for theta and 56% for delta (Feinberg et al., 2011). Thus, the maturational trajectories of the two main homeostatic frequencies, delta and theta, differ by age and topographic patterns, which most likely indicates that

the synaptic pruning in different brain regions is accomplished at different rates (Feinberg et al., 2011). Higher delta power in the frontal than in the occipital cortex could be attributed to the higher need for homeostatic recuperation in this cortical area that handles 'executive functions' (Luna and Sweeney, 2004; Kurth et al., 2010a; Feinberg et al., 2011).

The topographical frontal predominance of delta power during development is in agreement with MRI studies. Neuroimaging studies describe that brain maturation

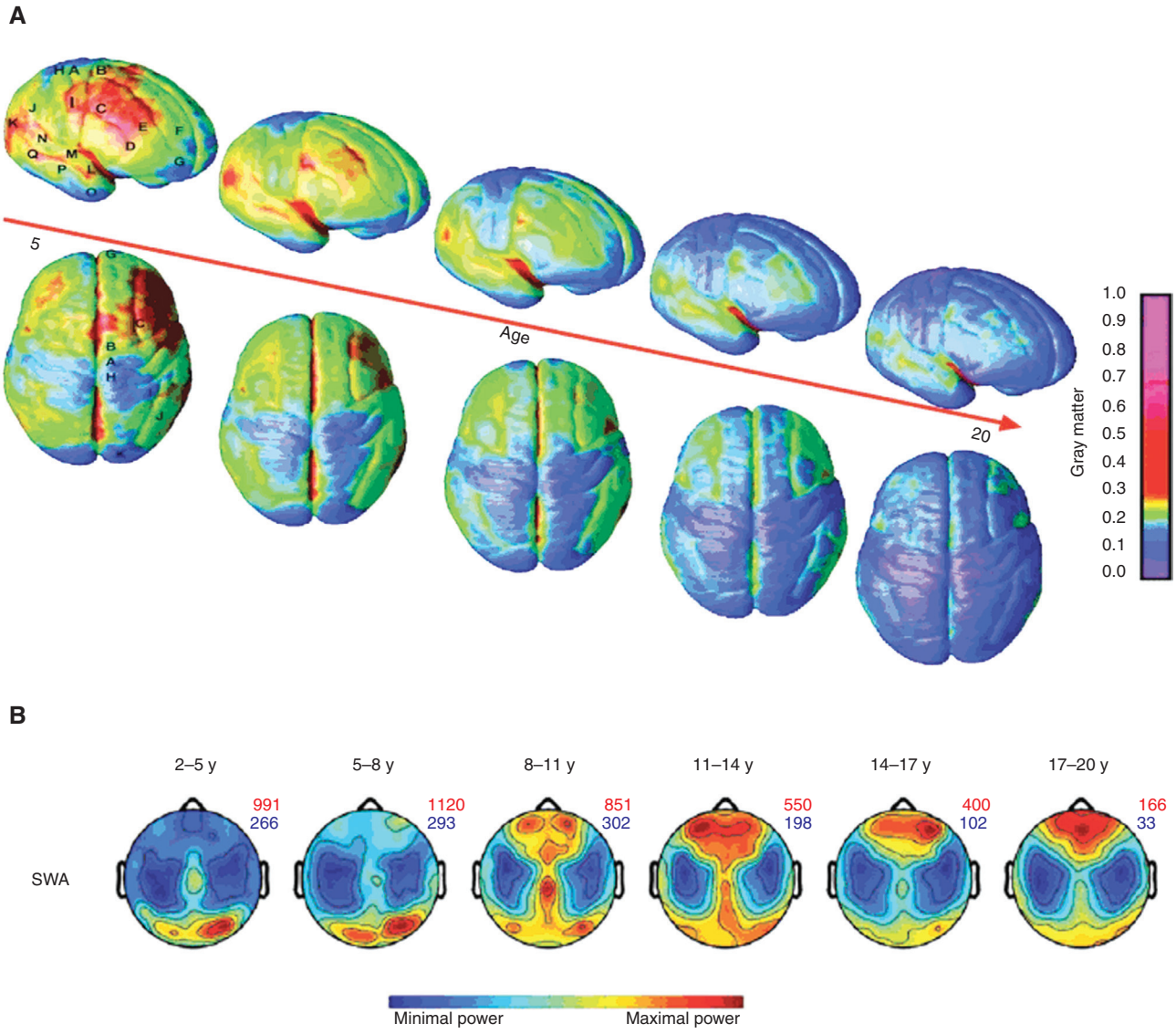

Figure 3 Brain maturation and SWA topography.
(A) Right lateral and top views of the dynamic sequence of GM maturation over the cortical surface. The side bar shows a color representation in units of GM volume. The initial frames depict regions of interest in the cortex: A, precentral gyrus and primary motor cortex; B, superior frontal gyrus, posterior end near central sulcus; C, inferior frontal gyrus, posterior end; D, inferior frontal sulcus, anterior end in the ventrolateral prefrontal cortex; E, inferior frontal sulcus in the dorsolateral prefrontal cortex; F, anterior limit of superior frontal sulcus; G, frontal pole; H, primary sensory cortex in postcentral gyrus; I, supramarginal gyrus (area 40); J, angular gyrus (area 39); K, occipital pole; L–N, anterior, middle, and posterior portions of STG; O–Q, anterior, middle, and posterior points along the inferior temporal gyrus anterior end. Reproduced from Gogtay et al. (2004). (B) Maps of EEG power during NREM sleep. Topographical distribution of NREM sleep EEG power for the defined age groups and frequency ranges (n=53). Maps are based on 109 derivations from the first 60 min of NREM sleep stages 2 and 3. Maps were normalized for each individual and then averaged for each age group. Values are color coded (maxima in red, minima in blue) and plotted on the planar projection of the hemispheric scalp model. To optimize contrast, each map was proportionally scaled, and values between the electrodes were interpolated. At the top right of the maps, numbers indicate maxima and minima (in square microvolts) for each plot. Adapted from Kurth et al. (2010a).

across childhood-adolescence follows a posterior-anterior maturational pattern across the cortex (Giedd, 2004; Gogtay et al., 2004; Sowell et al., 2004; Whitford et al., 2007; Shaw et al., 2008). The developmental decline in cortical gray matter, most likely reflecting pruning of synapses, occurs latest in the frontal cortex – the brain area with higher-order functions (Gogtay et al., 2004). In addition to MRI studies, it is noteworthy to report postmortem histological data that have also detected earlier decrease in synaptic density in the occipital than in the frontal cortex (Huttenlocher, 1979; Huttenlocher and Dabholkar, 1997). The region-specific pattern of the gray matter development from childhood through early adulthood detected in a longitudinal study by Gogtay and colleagues is presented in Figure 3A. More recent studies on regional differences in EEG maturation complete the overall picture about the back-to-front brain developmental pattern reflected in the delta EEG power decline. Kurth et al. (2010b) have explored age-related topographical changes in NREM sleep in 55 subjects (2.4–19.4 years) subdivided into six age groups with high-density (128 channel) EEG recordings. They found that SWA undergoes a shift from posterior to anterior regions across childhood and adolescence (Figure 3B), thus follows the similar time course as MRI measured cortical maturation (Figure 3A). Analogous age-related spatial changes were not detected for other frequency ranges. Mapping of SWA using high-density EEG also reveals an association between the structural maturation of cortical regions during childhood and adolescence and the maturation of SWA (Kurth et al., 2012). The similar pattern in topographical changes (timing and location) of SWA and MRI measured cortical maturation across adolescence supports the idea that SWA 'not only reflect global changes in synapse density but also mirror the regional aspects of cortical maturation' (Kurth et al., 2010a).

In summary, the similar pattern in topographical changes (timing and location) of SWA and MRI measured cortical maturation across adolescence provides further evidence that sleep SWA might reflect the underlying mechanism of brain maturation. Such evidence is of particular importance since it demonstrates the potential of EEG as a tool for assessment of neurodevelopmental changes across adolescence. Adolescence is a sensitive period for the emergence of many psychiatric disorders. The pathophysiology of these disorders is largely due to the malfunction/variations in the process of the synaptic pruning and the reorganization of neuronal circuits. Scientific arguments based on anatomical, EEG and MRI studies indicate that the association between the developmental changes in sleep EEG and normal developmental trajectory of synaptic remodeling could be established. The sleep EEG as a way to detect aberration from this trajectory becomes extremely important from clinical perspectives.

Conclusions

The data on sleep behavior and sleep EEG changes across adolescence, a period of profound transition in terms of physiologic, cognitive and psychosocial functioning, have accumulated greatly over the past few decades, making it difficult for anyone to cover all the findings in a single review. The current evidence indicates that the steep decline in delta EEG across adolescence not only reflects the process of brain remodeling driven by cortical synaptic pruning but also the regional aspects of cortical development. Evidence strongly suggests that age 11–17 years is the most extensive period for EEG changes. This period should be an important focus for future studies of adolescent brain maturation to look for insights into the several psychobehavioral health problems emerging during this critical period of development. Sleep EEG recordings as a possibility to monitor brain development noninvasively, without any medical risk, is a central and very important component of such studies.

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