Mind, Brain, Education, and Biological Timing

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ABSTRACT—Circadian rhythms, in particular the sleep–wake cycle, modulate most, if not all, aspects of physiology and behavior. Their impact on education has recently begun to be understood, including a clear positive relationship between sleep and learning. In fact, sleep deprivation, common to adolescents throughout the world, has a deep effect on academic performance, and this fact is often increased by inadequate school schedules. This special issue of *Mind, Brain, and Education* deals with the relation between biological rhythms and learning, as discussed in an International Mind, Brain, and Education Society meeting that took place in Erice, Italy in May 2007. The articles (with contributors from Brazil, Croatia, Sweden, Spain, United Kingdom, United States, and Argentina) cover several aspects of this fundamental link between timing and education and suggest strategies to optimize school and sleep schedules for a better quality of life and improved academic performance of students.

One of the key features in the world of education is timing, a concept that encompasses most teaching and learning activities. Moreover, this concept includes the search for the neural basis of time-related events, including time estimation and perception parameters, as well as the effect of periodic regulation of physiology and behavior in terms of biological clocks. The focus of the International Mind, Brain, and Education Society (IMBES) is to facilitate interdisciplinary collaborations in all fields relevant to education; in this sense, time and timing could be considered fundamental variables that connect the study of the brain and of learning capabilities. With this aim in mind, IMBES organized an International Symposium on “Basic and Applied Topics in Biological Rhythms and Learning,” which took place in the Ettore Majorana Center for Scientific Culture in Erice, Italy, May 22–26, 2007.

The main purpose of the meeting was to present and discuss ongoing research on the influence of chronobiology on learning processes and, more specifically, to assess the impact of biological rhythms on educational programs. Although there are significant cultural and geographical differences with respect to school timing and organization, another objective of this meeting was to propose a number of recommendations aimed at optimizing educational activities taking into account chronobiological principles tailored to diverse geographical situations.

There is a broad body of evidence demonstrating that timing (including both daily and seasonal components) significantly affects learning and memory mechanisms, both in laboratory and field conditions. In particular, biological rhythmicity undergoes a deep developmental modulation that can be studied in physiological or behavioral terms, as defined by *chronotypes*, that is, temporal preferences which characterize individuals as diurnal or “larks” and nocturnal or “owls.” According to this chronotype classification, it is clear that adolescents tend to be phase delayed with respect to their social activities, resulting in a putative desynchronization between their endogenous circadian rhythms and the imposed temporal structure of the schools.

Educational timing is a complex web of daily, weekly, and seasonal components. Indeed, the problems arising from different school schedules (i.e., morning, afternoon, or evening shifts) or even the gradual or abrupt changes that occur in different schooling periods can be analyzed not only with respect to the disruptions induced in the students’ physiology and behavior (such as profound changes and problems related to their sleep–wake cycle) but also directly to their academic performance. Moreover, the alternation of school days and weekends, as well as the holiday seasons, also affects the circadian structure of the students because they are subjected to chronic periodical changes between entrained and free-running situations that certainly affect cognitive abilities. In addition, the neural processing of different kinds of information might also vary throughout the day. Information

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about this differential acquisition of information can be useful for defining school schedules in terms of the different courses to be offered.

This special issue of *Mind, Brain, and Education* is devoted to selected aticles in the field that were specially prepared by some of the attendees to the Erice meeting. We are very grateful to the editors of the journal for this opportunity to share some concepts and findings of this growing chronobiological approach to educational processes. We believe that this issue is an interesting contribution for researchers across several disciplines including neuroscience, psychology, and education.

The aim of this introduction is to provide a general frame of chronobiology and sleep science and its relationship to learning and education processes.

BIOLOGICAL CLOCKS

Nested deep within the brain, a master biological clock guides our temporal organization. Part of a network of oscillators throughout the body, the hypothalamic suprachiasmatic nuclei (SCN) represent the tip of a clockwork iceberg, organizing the activity of "peripheral" clocks which are present in most tissues (Reppert & Weaver, 2002; Stratmann & Schibler, 2006). The circa 24-hr (circadian) activity of the SCN is coupled through neural and humoral pathways with output relay stations that control rhythmic behavior and physiology (Buijs et al., 2006). These circadian oscillations are entrained to diurnal cycles by environmental zeitgebers ("time givers") by daily stimulation of the clock. The most important of these signals is the light–dark cycle, which is transduced through a retinohypothalamic tract leading to a cascade of neurochemical and genetic changes in the SCN (Golombek et al., 2003). This entrainment–SCN–output pathway regulates chronobiological parameters, including the timing of the sleep–wake cycle (Zee & Manthena, 2007).

The molecular machinery sustaining circadian activity has been subjected to intense research in the past few decades. A series of transcription–translation feedback loops comprising both positive and negative elements (clock genes) are at the core of the biological clock and, moreover, the system provides output signals that are able to control the expression of other, clock-controlled, genes (Ko & Takahashi, 2006). Indeed, mutations of clock genes affect diverse parameters of the circadian system, including amplitude, period, and phase (or, in some extreme cases, render the system completely arrhythmic). It is interesting that some of these mutations have a profound effect on human behavior. The screening of genetic polymorphisms in human clock genes has reported correlations with alterations in sleep or diurnal preferences (Carpen, Archer, Skene, Smits, & von Schantz, 2005; Katzenberg et al., 1998; Mishima, Tozawa, Satoh, Saitoh, & Mishima, 2005). For example, in the delayed sleep phase syndrome (DSPS), a correlation with certain polymorphisms in the clock gene hPer3 has been found (Archer et al., 2003; Pereira et al., 2005), whereas a mutation in the hPer2 gene is associated with familiar advanced sleep phase syndrome (Toh et al., 2001). In addition, certain types of depression such as bipolar disorder might also be related to alterations in clock genes or their regulators (Mansour, Monk, & Nimgaonkar, 2005); moreover, depressed patients exhibit profound changes in their circadian rhythms, an alteration which might also predict the onset of symptoms (Bauer et al., 2006).

The study of human rhythms in behavior and cognitive functions has revealed that temporal preferences vary significantly among individuals and populations. In this sense, there is a characterization of circadian phenotypes based on their performance and preferences throughout the day, known as "chronotypes," varying from extreme matutine types (larks) to extreme vespertine types (owls), with the majority of the population residing between these two extremes (Horne & Ostberg, 1976; Zavada, Gordijn, Beersma, Daan, & Roenneberg, 2005). It is interesting to note that chronotyping—usually performed by means of specific questionnaires such as the Horne–Ostberg or the Munich questionnaires (Horne & Ostberg, 1976; Zavada et al., 2005)—has shown a predictable change with developmental age, varying from vespertine types during adolescence to early types in aged individuals (Mongrain, Carrier, & Dumont, 2006). Moreover, there have been some attempts to correlate chronotypes with circadian gene polymorphisms, which have been contradictory (Archer et al., 2003; Katzenberg et al., 1998; Pereira et al., 2005). Conflicts between social and biological timing (which have been collectively termed as "social jetlag") usually result from discrepancies between work/school days and free days, which lead to considerable sleep debt in a diversity of contemporary situations (Wittmann, Dinich, Merrow, & Roenneberg, 2006).

It is interesting to note that vespertine chronotypes, typically found in adolescents, define an important contrast with their daily duties and tasks, starting by the temporal schedules imposed by most school systems (Carskadon, Acebo, & Jenni, 2004; Giannotti, Cortesi, Sebastiani, & Ottaviano, 2002). As will be shown in this special issue of *Mind, Brain, and Education*, correct management of school schedules in diverse environments will result not only in an increase in the general health and quality of life but also in a significant improvement in their academic records and cognitive abilities. The first step toward adapting school and work schedules to individual/population chronotypes is, of course, to acknowledge the necessity of sleep for adequate human performance.

CIRCUITS MEDIATING WAKING AND SLEEP STATES

Sleep is divided into two states: rapid eye movement (REM) sleep and slow or non-REM sleep. These two states manifest very differently both inside and outside the central nervous system and appear to be regulated by different regions of the brain (Saper, Scammell, & Lu, 2005). Non-REM and REM sleep are defined by electroencephalographic brain wave patterns, amount of eye movement, and electromyography activity. In human subjects, sleep is usually consolidated into an 8-hr period during the night. In any typical sleep episode, the two substates alternate: in adult humans, the non-REM–REM sleep cycle has a period of 90–100 min (Pace-Schott & Hobson, 2002).

Although sleep rhythms can be disrupted by eliminating external cues, such as light–dark cycles, when those cues are available, sleep rhythms are stabilized, as are temperature rhythms and numerous other biological rhythms (Saper et al., 2005). It is a current opinion that the timing of sleep and wakefulness is mediated by two interconnected processes: a homeostatic regulatory process that increases during waking and decreases during sleep, together with a circadian clock-dependent mechanism (Pace-Schott & Hobson, 2002).

Experimental evidence indicates that sleep–wake cycles are controlled by a "switch" mechanism that is exerted by interactions of hypothalamic nuclei (reviewed in Saper et al., 2005). On the other hand, transitions between sleep and wakefulness have to be rapid and flawless; such transitions have been suggested to be controlled by wake-promoting and sleep-promoting nuclei in the hypothalamus and brainstem that are mutually inhibitory, forming a bistable switch that ensures rapid transitions between sleep and wakefulness with no in-between states (Saper et al., 2005).

Total sleep needs decrease from 14 to 16 hr/day in the newborn to approximately 8 hr/night by age 18 (Ohayon, Carskadon, Guilleminault, & Vitiello, 2004; Taylor, Jenni, Acebo, & Carskadon, 2005). One-year-old children sleep 11–12 hr/night with another 2.5 hr of sleep obtained in two separate daytime naps. By age 3, the average child gets 10.5 hr of sleep each night with one 1.5-hr nap. In Argentina, a typical child ceases daytime naps at about 4–5 years of age. There is considerable individual variation in sleep requirements as well as cultural influences on sleep and napping behavior. For example, daytime naps continue through adulthood in Latin American cultures. In the first regional survey on the prevalence of sleep disturbances in an urban Latin American population, two thirds of those surveyed, regardless of age and gender, reported some type of sleep problem within the last 12 months (Blanco, Kriber, & Cardinali, 2004). Although 8.2 hr of sleep is the desired standard, Latin Americans sleep on average about 2 hr less per night (Blanco et al., 2004).

REDUCTION OF SLEEP CAN IMPACT LEARNING

A very important general principle about the circadian system relevant to learning is that it adapts slowly to changes in sleep–wake schedules. Thus, adolescents who rapidly shift sleep–wake schedules between school nights and weekends or vacations face an impact on their circadian rhythms (Carskadon et al., 2004). Another important principle relevant to education is that the circadian system adapts more easily to delays in the sleep–wake schedule than to advances. This is the reason why it is naturally easier to stay up later and sleep in later on weekends and why it is easier to travel westbound rather than eastbound (Cardinali, Furio, Reyes, & Brusco, 2006; Hastings, Reddy, & Maywood, 2003).

The relevance of these principles to adolescent sleep patterns is paramount. Many adolescents have abrupt changes in the timing of their sleep between regular school schedules, requiring early morning awakening and late bedtimes due to social activities, leisure, and so on, causing quick shifts back to late bedtimes and sleeping in on weekends and vacations. For example, a typical Argentine adolescent goes to bed at 3:00 a.m. on weekends and sleeps in until noon. This will cause a phase delay in their circadian system within even 1–2 nights. However, the shift to an earlier waking time after a weekend, compatible with going to school early in the morning, will require several days of a stable schedule to shift the temperature and hormone rhythms completely back into a "normal" phase.

Inadequate sleep and sleep disordered breathing (SDB) can impair learning skills. A cross-sectional survey of students from seven schools in four cities of Argentina was conducted to evaluate the performance of a Spanish version of the Pediatric Daytime Sleepiness Scale (PDSS) to assess the impact of sleepiness and SDB on academic performance (Pérez-Chada et al., 2007). The sample included 2,884 students (50% males; age: 13.3 ± 1.5 years). Mathematics and language grades were used as indicators of academic performance. Half of the students slept less than 9 hr/night on weekdays. Reported snoring or apneas and daytime sleepiness as measured by the PDSS were significant univariate predictors of academic failure and remained significant in multivariate logistic regression analysis after adjusting for age, sex, body mass index (BMI), attending a specific school, or sleep habits (Pérez-Chada et al., 2007). In addition, BMI also correlated negatively with academic performance (Pérez-Chada, Drake, Pérez Lloret, Videla, & Cardinali, in press).

Therefore, many adolescents, particularly those who oversleep or miss an occasional day of school during the middle of the week, may experience jetlag–like symptoms (i.e., fatigue, difficulty in falling asleep at night, or difficulty in awakening in the morning). In the most severe cases, labeled DSPS, adolescents and their families often battle for months about late-night bedtimes and great difficulties awakening on school days. Indeed, these adolescents are pushed to awaken during their period of minimum body temperature, when their body is not prepared to be awake and active. Slow, steady, and consistent changes in sleep–wake timing will permit the circadian system to realign to a more appropriate pattern. However, conflicts between social timing (i.e., school or work schedules) and biological timing (i.e., individual sleep and rhythm characteristics) are deeply rooted in our culture, as can be judged from a historical perspective, although this misalignment tends to be larger in recent decades.

A BRIEF HISTORY OF TIMETABLES AND SCHOOL SCHEDULES

Most histories of school organization reserve a special place for Comenius' *Didactica Magna* (first published in 1640) (Comenius, 1986). In this work, a general reform for basic education is proposed, which means to establish a philosophical basis for teaching as well as practical implications to be considered at the different levels of schooling. Although Comenius does give advice on the management of school times and schedules, it is not until the 19th century that the distribution of timetables for education was established (Moreno Martínez, 2006). In general, school days tended to be organized in two 3-hr sessions, one in the morning and one in the afternoon, from Monday through Saturday. Classes were organized in consecutive 20- to 40-min sessions covering different subjects, which required a great effort of concentration and alertness by students, regardless of their educational age (Carderera y Potó, 1866). Indeed, when the beneficial effects of periodic breaks were discovered, thanks to a series of studies by Burgerstein (1887) and Ebbinghaus (1885) among others, assessing physical and mental performance with or without breaks in between (Binet & Henri, 1898), changes were made to design a more flexible curriculum.

However, no distinction was made for age-related changes in chronobiological parameters, a custom that is certainly maintained nowadays, when there is no transition in school schedules that accompany variations in the sleep–wake cycle (as well as other rhythms, including cognitive performance), resulting in a striking decrease in academic performance (Andrade, Benedito-Silva, Domenice, Arnhold, & Menna-Barreto, 1993; Carskadon, Wolfson, Acebo, Tzischinsky, & Seifer, 1998; Guerin et al., 2001; Yang, Kim, Patel, & Lee, 2005; several articles in this issue of *Mind, Brain, and Education*). Indeed, not only the physiological and developmental changes that affect the biological clock are responsible for this misalignment between social (i.e., school schedules) and biological (i.e., chronotypes) timing, but cultural influences—including nocturnal activities, such as chronic engagement in social networking—are deeply affecting performance in the general population, of which teenagers are especially at risk because of their unique chronobiological profiles.

SLEEP AND EDUCATION

We face an "environmental mutation." During the past century, life has changed dramatically and the necessity of physical effort has become considerably reduced. In addition, physical activity no longer needs to coincide with daylight hours (i.e., the "24-hr society"). Food has become abundant in most countries, snacking frequency has increased, and mealtime has shifted toward the end of the day. As a result, the environment sensed by the brain has become metabolically flattened and arrhythmic. From an evolutionary perspective, this has been an abrupt environmental mutation. In such conditions, the brain has reduced its capability to sense internal and external rhythms (Kreier et al., 2003). A very important factor is the decrease in the hours of sleep in most modern societies, including Latin America (Blanco et al., 2004). It is estimated that we have lost 25% of sleep hours in just 40 years, mainly because of the radical changes in social behavior and technology brought about by the 24-hr society. At steady state in artificial long nights, normal volunteers sleep an average of 8.25 hr/night, which is more than most humans obtain in modern life. From this finding, it is certain that modern humans are sleep deprived and less fully awake in the daytime than would otherwise be the case (Copinschi, 2005; Siegel, 2005).

In summary, the present special issue of *Mind, Brain, and Education* deals with a fundamental problem in terms of contemporary quality of life: the lack of an adequate sleep cycle that enables full diurnal alertness. One of the most striking consequences of this debt is seen in adolescent school performance, which could be greatly improved if accommodated to their developmental and chronobiological stage.

The five articles in this special issue of *Mind, Brain, and Education* cover different aspects of the relationship of chronobiology/sleep research and education. It is interesting that several of the articles represent collaborations between groups of different countries and even continents. We have organized the articles to begin with a focus on basic biology and then move toward connections to educational practice. The first article, by Valdez, Reilly, and Waterhouse, from the University of Nuevo León (Mexico) and Liverpool John Moores University (United Kingdom), reviews diurnal and circadian rhythms in several tests of mental performance, which also depend on the consequences of fatigue. Sleep, wakefulness, and circadian phase, therefore, interact and are deeply connected to alertness levels which are fundamental for students' performance. The article in this issue by Fischer et al. (which represents collaboration between groups from Brazil, Croatia, and Sweden) goes directly into the effects of sleep habits in adolescents' performance, in particular related to school schedules and the burden of extra work on teenagers' health and alertness. The following contribution, by Menna-Barreto and Wey (from the University of Sao Paulo, Brazil), goes more deeply into the problem of school schedules and their effect on performance; the authors argue for the urgent need to reconsider time planning in the school setting.

The article in this issue by Miller et al. gives an extreme example of the effect of school schedules and sleep deprivation on mental and physical performance. They analyze the effects of military training regimes (which usually include a certain degree of sleep deprivation) on sleep–wake schedules and academic performance of the students.

Finally, in another multinational contribution (with groups from Brazil, Spain, and the United States), the article by Azevedo et al. shows another aspect of the relationship between chronobiology/sleep research and education. They present examples of the effects of teaching chronobiology and good sleep habits on the academic performance and general well-being of students of different ages. Although the results exhibit some variability, these exercises underscore the potential power of good education about sleep, in particular in this risk-prone age span.

In summary, the articles of this special issue of *Mind, Brain, and Education* support the idea of a strong connection between chronobiology/sleep research and education, in particular, in terms of learning in adolescents as related to their sleep–wake schedules. Indeed, a broad body of evidence supports the positive relation between sleep and learning. This relation has a deep impact on not only the scientific research but also the quality of life and academic performance of students. The concepts of time and timing—deeply controlled by the brain—need to be incorporated into any general view of educational processes.

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