Chapter 10

Evolution of Mammalian Sleep

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Chapter Highlights

- In most adult animals, sleep is incompatible with mating and feeding. Animals seem to be vulnerable to predation during sleep. Why has evolution preserved this state? I conclude that the presence of sleep in nearly all animals and the enormous variation in sleep time across species is best explained as an adaptation to ecological and energy demands.
- Sleep is not a "maladaptive state" that needs to be explained by undiscovered functions (which nevertheless undoubtedly exist). Genetic success is closely linked to the efficient use of resources and to the avoidance of risk. Thus inactivity can reduce injury, and safe sleeping sites reduce predation. Sleep greatly reduces brain and body energy consumption. In the wild, most animals are hungry and are seeking food most of the time they are awake. If ample food is available, the population of a species quickly expands until again faced with food scarcity, a phenomenon that is illustrated by the great increase in the human population in the past century. A "small" energy saving every day produces a big evolutionary advantage.
- Conversely, if food is available but is time consuming to acquire, it is advantageous for animals to reduce sleep time. Similarly, it is advantageous to reduce or eliminate sleep to allow migration and respond to other needs. Many examples of extended periods of elimination or sleep reduction without "rebound" have been documented.
- Many have assumed that predation risk is increased during sleep; that is, that more animals are killed per hour during sleep than during waking. However, there is scant evidence to support this contention. Most animals seek safe sleeping sites, often underground, in trees or in groups that provide communal protection. Those large herbivores that cannot find safe sleeping sites appear to have smaller amounts of sleep and sleep less deeply. Large animals that are not at risk for predation, such as big cats and bears, can sleep for long periods, often in unprotected sites, and appear to sleep deeply.
- Much has been made of mathematical analyses comparing reported sleep time across species with other aspects of comparative each species. For example, total sleep time or REM sleep time is compared with body weight, brain-body weight ratio, and lifespan. The available sleep parameters generally come from studies of animals in controlled environments in laboratories or zoos. Such analyses have been undermined by recent work showing that sleep time varies substantially with season, temperature, migration, age, and breeding phase. Conversely, the constant temperature conditions, complete lack of predatory risk, and ad libitum food and water availability in captivity are almost never experienced in the wild and undoubtedly are major factors controlling the evolution of sleep. A complete understanding of sleep evolution requires analyses of sleep under the actual conditions in which each species evolved and continues to live. Fortunately, advances in electronics now make such studies more practical and will lead to a better understanding of the evolutionary determinants of sleep.
- "Natural" human sleep, as observed in human hunter-gatherers, does not commence at sunset, is not normally interrupted by extended waking periods, is somewhat shorter in duration than that in industrial societies, and shows a nearly 1-hour difference between summer and winter. Napping is not a regular feature of hunter-gatherer sleep, and insomnia is rare.

ADAPTIVE INACTIVITY

Sleep should be viewed in the context of other forms of "adaptive inactivity." Most forms of life have evolved mechanisms that permit the reduction of metabolic activity for long periods of time when conditions are not optimal. In animals, this usually includes a reduction or cessation of movement and sensory response. The development of dormant states was an essential step in the evolution of life and continues to be essential for the preservation of many organisms. Many species have evolved seasonal dormancy or hibernation patterns

that allow them to anticipate periods that are not optimal for survival and propagation. In other species dormancy is triggered by environmental conditions. Many organisms spend most of their lifespan in dormancy, becoming active only when conditions are optimal. A continuum of states of adaptive inactivity can be seen across living organisms including plants, unicellular and multicellular animals, and animals with and without nervous systems.[1]

In the plant kingdom, seeds are often dormant until the correct season, heat, moisture, and pH conditions are present. One documented example of this was a lotus seed that produced a healthy tree after a 1300-year period of dormancy.[2] Another was a 2000-year-old date palm seed that produced a viable sapling.[3] Some forms of vegetation can germinate only after fires that may come decades apart. These include the giant sequoias native to the US southwest. Most deciduous trees and plants have seasonal periods of dormancy during which they cease photosynthesis, a process called abscission.

A tiny colony of yeast trapped inside a Lebanese weevil covered in ancient Burmese amber for up to 45 million years has been reported to have been brought back to life and used to brew a modern beer.[4] Rotifers, a group of small multicellular organisms, have extended dormant periods lasting from days to months in response to environmental stresses, including lack of water or food.[5,6] Parasites can become dormant within an animal's tissues for years, emerging during periods when the immune system is compromised.[7] Some invertebrate parasites have extended dormant periods, defending themselves by forming a protective cyst.[8] Insect dormancy or diapause can be seasonal, lasting several months, and anecdotal reports indicate that, under some conditions, can last for several years to as long as a century.[9] This can occur in an embryological, larval, pupal, or adult stage. During diapause insects are potentially vulnerable to predation, as are some sleeping animals. Passive defense strategies are employed, such as entering dormancy underground or in hidden recesses, having hard shells, and tenacious attachment to substrates. Land snails and slugs can secrete a mucus membrane for protection and enter a dormant state.[10]

Reptiles and amphibia that live in lakes that either freeze or dry seasonally and snakes that live in environments with periods of cold or extreme heat have the ability to enter dormant states. These may occur just during the cool portion of the circadian cycle or may extend for months in winter.[11] Estivation is a form of dormancy that occurs during warm periods. It allows reptiles, amphibia, fish, and insects[12-16] to emerge with the first rains from what had been a dry, apparently lifeless environment.

In the mammalian class, a continuum of states ranging from dormancy to continuous activity can be seen. Small animals that cannot migrate long distances and live in temperate or frigid environments often survive the winter by hibernating. Some bats, many species of rodents, marsupials, and insectivores hibernate. This condition is entered from, and generally terminates in, non–rapid eye movement (NREM) sleep. During hibernation, body temperature can be reduced to below 10° C to as low as -3° C (with antifreeze protection).[17,18] Animals are quite difficult to arouse during hibernation, with full arousal taking as long as 2 hours. Consequently, hibernators are vulnerable to predation and survive hibernation by seeking protected sites. Torpor[17] is another form of dormancy that can be entered by mammals and birds daily. Torpor is entered and exited through NREM sleep and can recur in a circadian rhythm or can last for weeks or months. Animals in shallow torpor are less difficult to arouse than hibernating animals but are still unable to respond quickly when stimulated. Some other mammals such as bears have extended periods of sleep in the winter during which their metabolic rate and body temperature are reduced by 4° to 5° C,[19] but they remain more responsive than animals in torpor.

Sleep can be seen as a form of adaptive inactivity lying on this continuum. What is most remarkable about sleep is not the unresponsiveness or vulnerability it creates but rather its ability to reduce activity and body and brain metabolism, but still allow a high level of responsiveness relative to the states of dormancy described earlier in this chapter. The often cited example of a parent arousing at a baby's whimper but sleeping through a thunderstorm illustrates the ability of the sleeping human brain to continuously process sensory signals during the sleep period and trigger complete awakening to significant stimuli within a few hundred milliseconds. This capacity is retained despite the great reduction in brain energy consumption achieved in sleep relative to quiet waking.[20,21]

Adolescent humans are less responsive than adults to stimuli presented during sleep, as anyone who has raised teenagers can attest. This may have been selected for by evolution, because protection from predators is provided by older members of the family group who also tend to the nocturnal needs of infants. The inactivity of children benefits the group by reducing their relatively large portion of the family's food needs and diverting food energy to growth.

Some animals that live in climates with seasonal reduction in food or light availability or a periodic increase in threat from predators have evolved migration to survive. Many species of birds do this, as do certain species of marine mammals (see the section Marine Mammals). Although some may maintain circadian rhythms of activity during migration, others remain continuously active for weeks or months. Some vertebrates do not ever appear to meet the behavioral criteria for sleep, remaining responsive, or responsive and active, throughout their lifetime.[22]

Humans with a complaint of "insomnia" are typically not sleepy during the day, despite a reduced (or in many cases normal) duration of nighttime sleep. They may be viewed as falling closer to migrating animals or short-sleeping animals, in contrast to humans with sleep disturbed by sleep deprivation, sleep apnea, or pain, who are sleepy during the day.[23] Conversely, many individuals with hypersomnia appear to need more sleep and sleep more deeply, rather than being the victims of a shallow or disrupted sleep that is compensated for by extended sleep time. Perhaps these individuals may be expressing genes and a behavior that was highly adaptive for reducing energy consumption.

QUANTITATIVE ANALYSES OF THE CORRELATES OF SLEEP DURATION IN MAMMALS

Mathematically inclined researchers have attempted to correlate the data that have been collected on sleep duration in mammals with physiologic and behavioral variables in order to develop hypotheses as to the function of sleep. However, the data these studies are based on are not ideal. Only approximately 80 mammalian species have been studied with sufficient measurements to determine the amounts of rapid eye movement (REM) and NREM sleep over the 24-hour period. These are by no means a random sample of the more than 5000

mammalian species. Rather they are species that are viable and available for study in laboratories or in some instances for noninvasive (and less accurate) studies in zoos. In laboratories, animal subjects for sleep studies are typically fed ad libitum; are at relatively invariant, thermoneutral, temperatures; and are on artificial (usually 12-12) light-dark cycles. These environments differ greatly from those in which animals evolved. Digital recording and storage technologies now exist that will enable the collection of polygraphic data on animals in their natural environments.[24] An excellent example is a 2018 study by Davimes and colleagues of the Arabian oryx under natural conditions. This animal shows a major seasonal difference in sleep duration (6.7 hours in winter and 3.8 hours in summer), and the circadian timing of its sleep differs greatly across the seasons.[25] Such "natural" observations are necessary to determine the variation in sleep times caused by hunger, response to temperature changes, predation, and the other variables that have driven evolution. Very few animals whose sleep has been studied have been tested for arousal threshold, the nature and extent of sleep rebound, and other aspects of sleep whose variation across species would contribute to an understanding of sleep evolution and function. In humans, we know that sleep depth, as assessed by either arousal threshold or electroencephalogram (EEG) amplitude, increases after sleep deprivation. Can sleep time be profitably compared across animals without incorporating information on sleep depth[26]?

One of the earliest studies comparing REM and NREM sleep durations with physiologic variables found that sleep duration was inversely correlated with body mass.[27,28] Our subsequent analysis found that this relationship applied only to herbivores, not to carnivores or omnivores.[29] This study also showed that, as a group, carnivores slept more than omnivores, who in turn slept more than herbivores (Figure 10.1). In an early study, a significant negative correlation was found

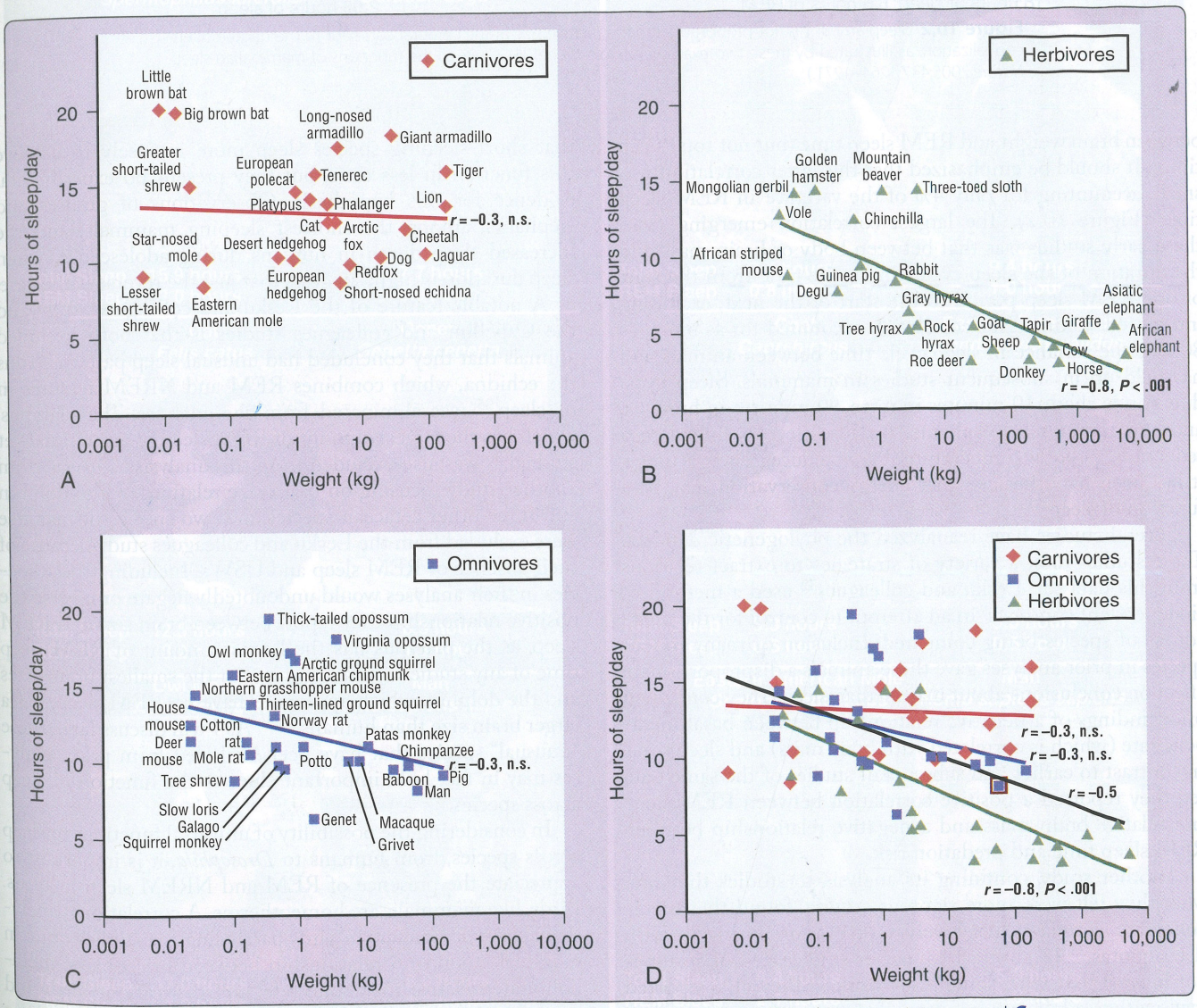

Figure 10.1 Sleep time in mammals. **A,** Carnivores are shown in dark red; **B,** herbivores are in green; and **C,** omnivores are in gray. Sleep times in carnivores, omnivores, and herbivores differ significantly, with carnivore sleep amounts significantly greater than those of herbivores. Sleep amount is an inverse function of body mass over all terrestrial mammals *(black line)*. This function accounts for approximately 25% of the interspecies variance **(D)** in reported sleep amounts. Herbivores are responsible for this relation because body mass and sleep time were significantly and inversely correlated in herbivores but were not in carnivores or omnivores. (From Siegel JM. Clues to the functions of mammalian sleep. *Nature* 2005;437:1264–1271.)

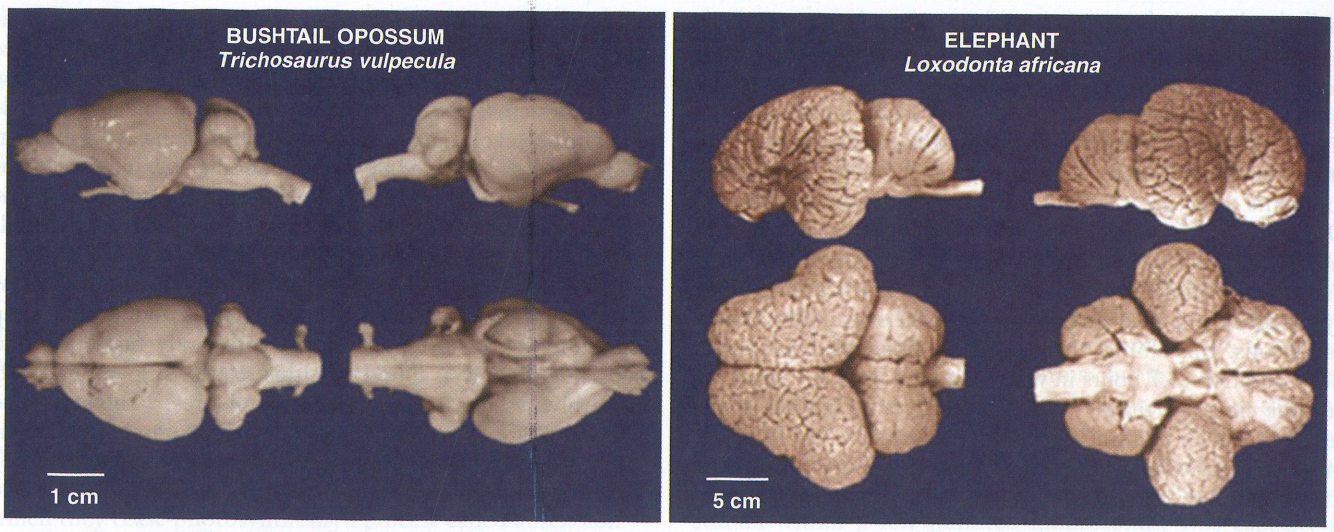

Figure 10.2 Sleep amount is not proportional to the relative size of the cerebral cortex or to the degree of encephalization, as illustrated by these two examples. (From Siegel JM. Clues to the functions of mammalian sleep. *Nature* 2005;437:1264–1271.)

between brain weight and REM sleep time (but not total sleep time). It should be emphasized that this latter correlation was small, accounting for only 4% of the variance in REM sleep time (Figure 10.2). The largest correlation emerging from these early studies was that between body or brain mass and the duration of the sleep cycle, that is the time from the start of one REM sleep period to the start of the next, excluding interposed waking. This correlation accounted for as much as 80% of the variance in sleep cycle time between animals and has held up in subsequent studies in mammals. Sleep cycle duration is about 10 minutes in mice, 90 minutes in humans, and 120 minutes in elephants. Because sleep is linked to a reduction in body temperature[30] and reduces energy usage, it has been hypothesized that energy conservation may be a function of sleep.[31]

Several studies have reanalyzed the phylogenetic data set. These studies took a variety of strategies to extract relations from this data set. Lesku and colleagues[32] used a method of "independent contrasts" in an attempt to control for the relatedness of species being compared. Inclusion of many rodent species in prior analyses gave these animals a disproportionate effect on conclusions about mammalian sleep. They confirmed prior findings of a negative relationship between basal metabolic rate (which is correlated with body mass) and sleep time. In contrast to earlier and subsequent studies of the same data set, they reported a positive correlation between REM sleep and relative brain mass and a negative relationship between REM sleep time and predation risk.

Another study, confining its analysis to studies that met what they felt were more rigorous criteria, found that metabolic rate correlates negatively rather than positively with sleep quotas,[33] in contrast to earlier studies.[28] This result is not inconsistent with some prior work.[29] They also reported that neither adult nor neonatal brain mass correlates positively with adult REM or NREM sleep times, differing from earlier studies.[28,33] They find, in agreement with prior analyses, that animals with high predation risk sleep less.[29,34] In keeping with the concept that there is some fixed need for an unknown function preformed only during sleep, they propose that short-sleeping species sleep more intensely to achieve this function in less time, but they present no experimental evidence for this hypothesis. Observations of giraffes and elephants, among the shortest sleeping mammals, and the increased sleep depth in humans during adolescence, when sleep duration is high, suggests that just the reverse is the case.

A notable feature of the Lesku and colleagues study and the Capellini and colleagues studies is that both excluded animals that they concluded had unusual sleep patterns. Thus the echidna, which combines REM and NREM features in its sleep,[35] was eliminated from the analyses. The platypus, which has the largest amount of REM sleep of any animal yet studied,[36] was also excluded from this analysis as it was from another study focusing on brain size relations.[37] The dolphin and three other cetacean species and two species of manatee were excluded from the Lesku and colleagues study because of their absence of REM sleep and USWs. Including these species in their analyses would undoubtedly negate or reverse the positive relationship they report between brain size and REM sleep, as the platypus has the largest amount of REM sleep time of any studied animal and one of the smallest brain sizes and the dolphin, which appears to have no REM sleep, has a larger brain size than humans.[38,39] As I will discuss later, these "unusual" species that have been excluded from prior analyses may in fact hold important clues to the function of sleep across species.

In considering the possibility of universal functions of sleep across species, from humans to *Drosophila*, it is important to appreciate the presence of REM and NREM sleep in birds. Birds, like mammals, are homeotherms. A correlational analysis of sleep parameters in birds paralleling the studies done in mammals found no relationship between brain mass, metabolic rate, relative metabolic rate, and maturity at birth and total sleep time or REM sleep time.[40] All relations of these parameters were found to be "markedly nonsignificant." The only significant relation found was a negative correlation between predation risk and NREM sleep time (but not REM sleep time), in contrast to the relation reported earlier in this chapter in mammals between predation risk and REM sleep

time (but not NREM sleep time). This lone significant relation explained only 27% of the variance in avian NREM sleep time.

To summarize, a variety of correlation studies, most done under laboratory or zoo conditions, reach disparate and often opposite conclusions about the physiologic and functional correlates of sleep time. It should be emphasized that with the exception of the strong relationship between sleep cycle length and brain and body mass, all of the "significant" correlations reported explain only a small portion of the variance in sleep parameters, throwing into question whether the correlational approach is getting at the core issues of sleep function. Despite similar genetics, anatomy, cognitive abilities, and physiologic functioning, closely related mammalian species can have very different sleep parameters and distantly related species can have very similar sleep parameters. Many such examples exist despite the relatively small number of species in which REM and NREM sleep time have been determined (Figure 10.3). For example, the guinea pig and baboon have the same daily amounts of REM and NREM sleep.[41]

THE DIVERSITY OF SLEEP

On the assumption that sleep satisfies an unknown yet universal function in all animals, some work has been carried out on animals whose genetics and neuroanatomy are better

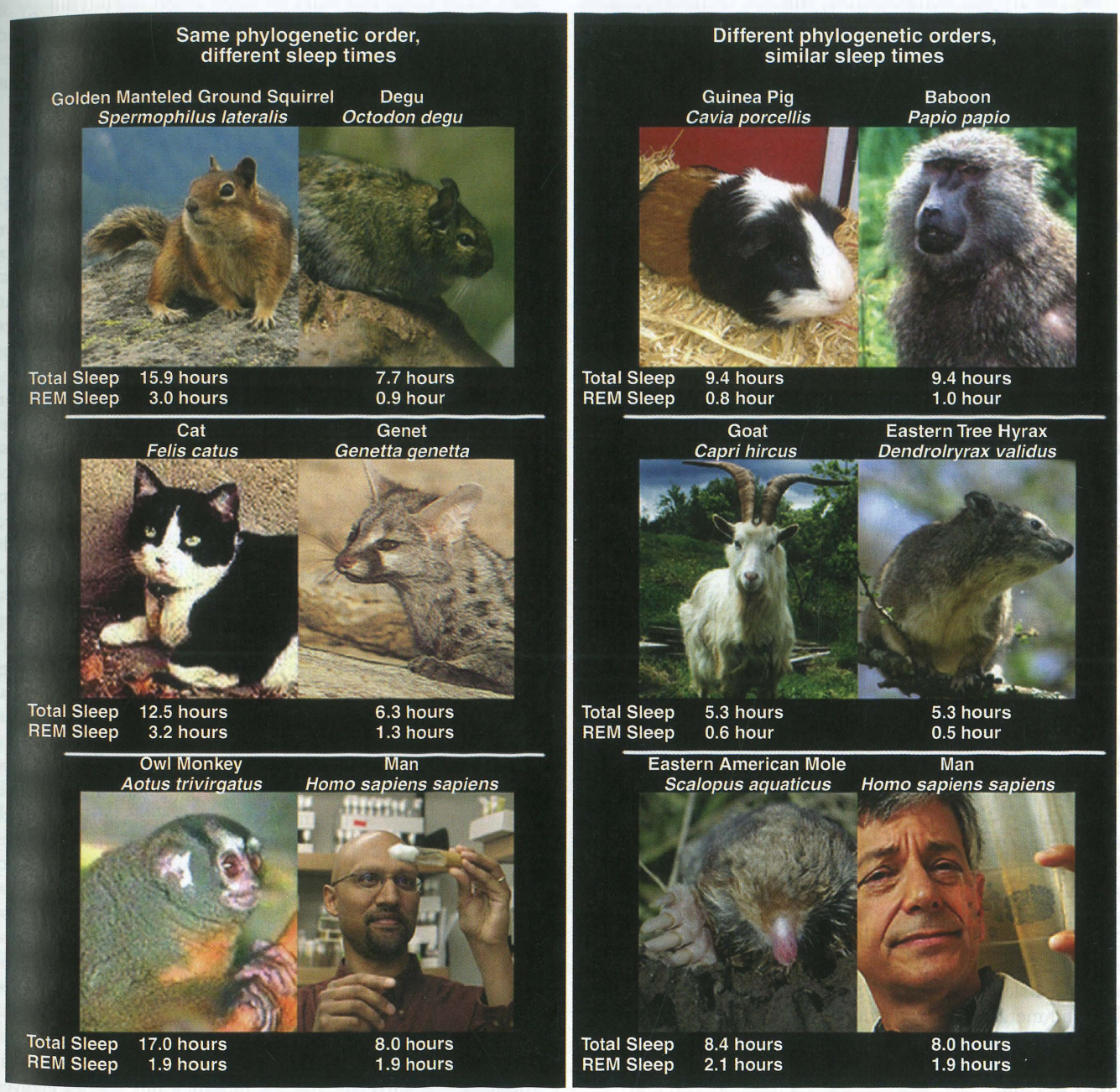

Figure 10.3 Mammalian phylogenetic order is not strongly correlated with sleep parameters. On the left are three pairs of animals that are in the same order but have very different sleep parameters. On the right are three pairs of animals from different orders with similar sleep amounts. Mammalian sleep times are not strongly correlated with phylogenetic order. (From Allada R, Siegel JM. Unearthing the phylogenetic roots of sleep. *Curr Biol.* 2008;18:R670–R679.)

understood and more easily manipulated than those of mammals. Much of this work has focused on the fruit fly, *Drosophila melanogaster*. These animals appear to meet the behavioral definition of sleep. Their response threshold is elevated during periods of immobility, but they will rapidly "awaken" when sufficiently intense stimuli are applied. They make up for "sleep" deprivation with a partial rebound of inactivity when left undisturbed. However, major differences between the physiology and anatomy of these organisms and those of mammals make it difficult to transfer insights gleaned from studies of *Drosophila* sleep to human sleep. The *Drosophila* brain does not resemble the vertebrate brain. Hypocretin, a major sleep regulating transmitter in mammals, does not exist in *Drosophila*.[41] *Drosophila* are not homeotherms, whereas thermoregulation has been closely linked to fundamental aspects of mammalian sleep[29,30,43] and they do not have REM sleep. Two studies have shown that *Drosophila* sleep and sleep rebound is markedly impaired by genetic alteration of a potassium current that regulates neuronal membrane excitability.[44,45] Regulation of potassium currents may be a core function of sleep or it simply may affect the excitability of circuits regulating activity and quiescence, just as such currents affect seizure susceptibility.[46,47]

A 2019 paper by Leung and colleagues claimed to detect a REM sleep-like state in larval zebrafish.[48] However, there have been no reports or REM sleep in adult zebrafish, or in any other fish species, to my knowledge. Arousal thresholds and homeostatic regulation were not demonstrated in larval zebrafish, so it is not clear that the described state is sleep, much less REM sleep. *Caenorhabditis elegans,* a roundworm with a nervous system much simpler than that of *Drosophila*, has also been investigated for sleep-like behavior.[49] *C. elegans* reaches adulthood in 60 hours and has periods of inactivity during this maturation called "lethargus" occurring before each of the four molts it undergoes before reaching maturity. Stimulation of *C. elegans* during the lethargus period produced a small but significant decrease in activity during the remainder of the lethargus period, but did not delay the subsequent period of activity or increase quiescence overall, phenomena that differ from the effects of sleep deprivation in mammals. It is not clear if adult *C. elegans* shows sleep behavior.[50]

Fundamental species differences in the physiology and neurochemistry of sleep have been identified even within the mammalian line. Although there are many similarities, the EEG aspects of sleep also differ considerably between humans, rats, mice, and cats, the most studied species.[51-53] Human stage 4 NREM sleep (N3 in the newer nomenclature) is linked to growth hormone secretion. However, in dogs, growth hormone secretion normally occurs in waking, not sleep.[54] Melatonin release is maximal during sleep in diurnal animals but is maximal in waking in nocturnal animals.[55] Erections have been shown to be present during REM sleep in humans and rats[56]; however the armadillo has erections only in NREM sleep.[57] Dolphins do not have REM sleep. Blood flow and metabolism differ dramatically between neocortical regions in adult human REM sleep,[58] although most animal sleep deprivation and sleep metabolic studies treat the neocortex as a unit.

Animal Dreaming?

Lesions of the parietal cortex and certain other regions eliminate dreaming recall in humans, even in individuals that continue to show normal REM sleep as judged by cortical EEG, rapid eye movements, and suppression of muscle tone.[59] Humans before age 6 do not generally report dream mentation, perhaps because these cortical regions have not yet developed.[60] These findings make it questionable whether nonhuman mammals that have REM sleep, all of which have cortical regions whose structure differs from that of adult humans, have dream mentation. We have reviewed data on REM and NREM sleep duration in mammals in the context of species differences in the anatomy of structures linked to REM sleep control.[61] We speculated on the possibility that certain species dream, emphasizing that we cannot know whether animals dream, regardless of whether or not they have REM sleep. But what we know about the physiology of sleep in different species suggests that some, such as cats and dogs, may dream, whereas others, such as cetaceans (whales and dolphins—animals that have the largest brains on our planet) are very unlikely to dream.

Elephants and Sloths

The sleep of elephants is of great interest. They are the largest land mammals, with the largest brain of any land mammal and one of the longest mammalian life spans. They have social structures and behaviors that rival those of primates in their complexity. In the wild they travel daily to find optimal resources of grasses, plants, bushes, fruit, twigs, and roots to eat. Typically the matriarch will lead the herd. She has to navigate to regions where the herd has not fed recently, a prodigious task and one consistent with the aphorism that "an elephant never forgets." Current theories postulating a strong relation of sleep to cognitive factors, life span, and health might suggest longer sleep durations in elephants than in animals with less social structure and lesser memory requirements. Yet studies of elephants in captivity had concluded that Asiatic elephants sleep only 4 to 6.5 hours a day.[62] Similar results were reported in a second study of captive elephants.[63] In our recent study we recorded from two wild African elephants in Botswana for 35-day periods. Satellite tracking revealed that they traveled as far as 45 km/day, averaging 15 km/day. We monitored sleep behavior by recording periods where the trunk was not moving, indicative of rest or sleep periods. We found that average rest periods were 2 hours per day. Even if all of these quiescent periods are sleep the amount is far lower than sleep times in captivity and are the lowest of any mammal (Figure 10.4), a challenge for theories that sleep duration is linked to cognitive or social structure factors. But from a behavioral standpoint it should not be too surprising that elephants in captivity, which have a bale of hay tossed into their enclosure in the morning, sleep more than elephants that have to walk 15 km a day on average to acquire food; that is elephants in zoos rest or sleep more because they do not need to be active. A similar phenomenon is seen when comparing sloths in captivity to those in the wild. Sloths in the wild sleep much *less* than sloths in captivity.[24,64] More species need to be examined in natural environments to determine whether this is a common or universal pattern. But our results in human hunter-gatherers (see the section Humans) suggest that humans living in the environment and with the lifestyle in which our species evolved also have lower sleep durations than humans in industrialized societies, notwithstanding the common assumption that industrial society and its electric lights have greatly reduced human sleep time below its "natural" level.

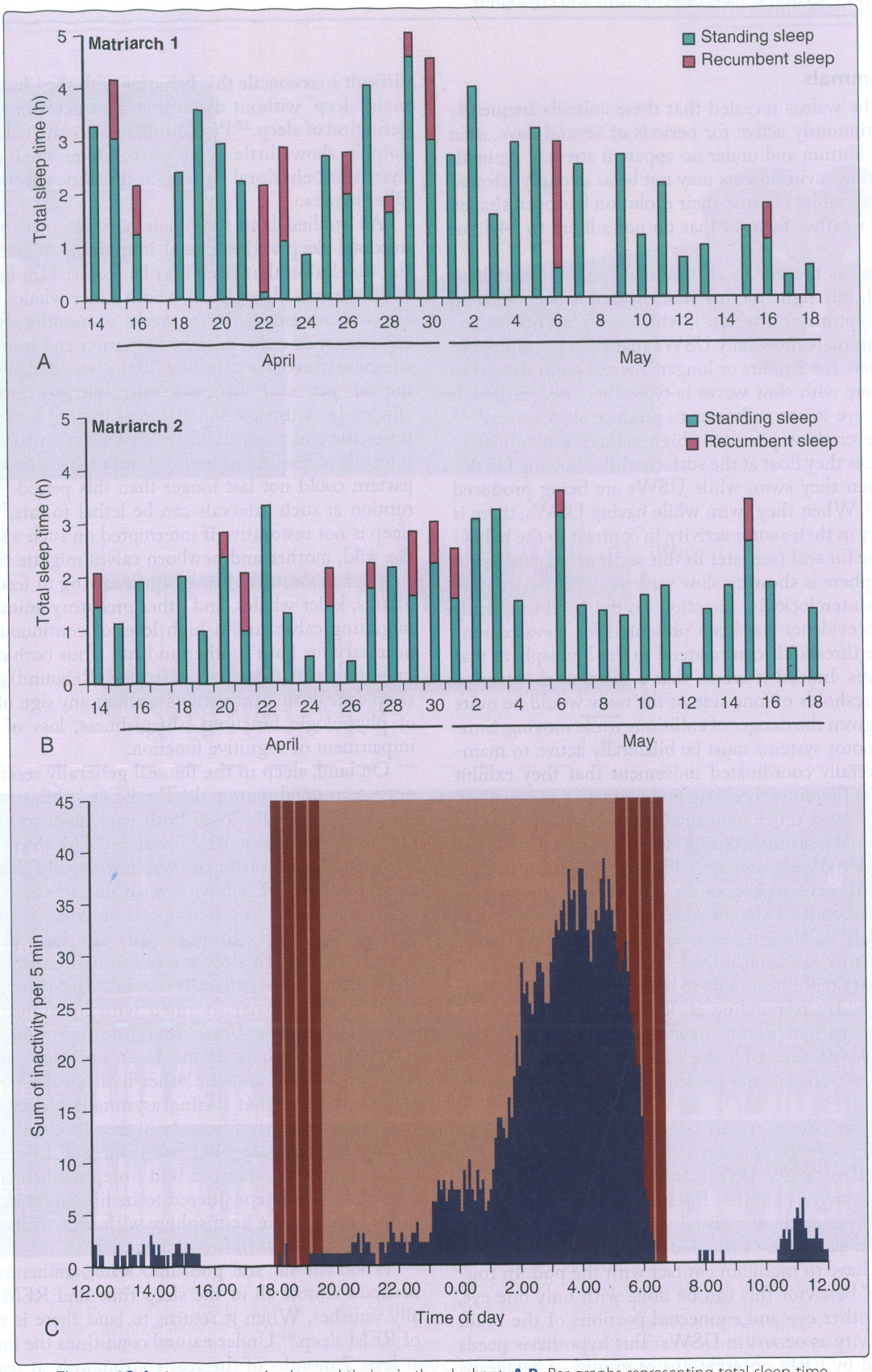

Figure 10.4 Sleep times, episodes, and timing in the elephant. **A,B,** Bar graphs representing total sleep time on each day through the 35-day recording period for each elephant. **A,** Matriarch 1; **B,** Matriarch 2. Note that on certain days no sleep was observed. The bars also represent the amount of time spent in standing sleep (blue) and in recumbent sleep (purple), although recumbent sleep did not occur on each day. **C,** Graph illustrating the average count of inactivity/sleep episodes for any given 5-minute period scored over the 35-day recording period and combining the data from both elephants. Note the clearly nocturnal pattern of inactivity, with little inactivity occurring during the daytime. The vast majority of sleep episodes occurred in the early morning during the hours of 02:00 and 06:00. The gray region represents the period between sunset (ss) and sunrise (sr). h, hour. (Gravett et al, 2017 Elephant.)

Marine Mammals

A study of the walrus revealed that these animals frequently become continuously active for periods of several days, even when fed ad libitum and under no apparent stress.[65] Animals living in marine environments may not be as strongly affected by circadian variables because their evolution has been shaped by tidal and weather features that do not adhere to 24-hour cycles.

REM sleep is present in all terrestrial animals that have been studied, but signs of this state have not been seen in cetaceans (dolphins and whales), which are placental mammals. These animals show only USWs that can be confined to one hemisphere for 2 hours or longer. The eye contralateral to the hemisphere with slow waves is typically closed, although covering the eye is not sufficient to produce slow waves.[36,66] Cetaceans never show persistent high-voltage waves bilaterally. Sometimes they float at the surface while showing USWs. However, often they swim while USWs are being produced (Figure 10.5). When they swim while having USWs, there is no asymmetry in their motor activity, in contrast to the behavior seen in the fur seal (see later in this section). Regardless of which hemisphere is showing slow wave activity, they tend to circle in a counterclockwise direction (in the northern hemisphere[67]). No evidence has been presented for elevated sensory response thresholds contralateral to the hemisphere that has slow waves. Indeed it seems that a substantial elevation of sensory thresholds on one side of the body would be quite maladaptive given the danger of collisions while moving. Similarly, brain motor systems must be bilaterally active to maintain the bilaterally coordinated movement that they exhibit during USWs. Therefore forebrain and brainstem sensory and motor activity must differ radically during USWs from that seen in terrestrial mammals during sleep (Chapter 8[68,69]). The one study of USW rebound after USW deprivation in dolphins produced very variable results, with little or no relation between the amount of slow waves lost in each hemisphere and the amount of slow waves recovered when the animals were subsequently left undisturbed.[70] In two other studies it was shown that dolphins are able to maintain continuous vigilance 24 hours/day, responding at 30-second intervals, for 5 and for 15 days with no decline in accuracy. At the end of this period there was no detectable decrease of activity or evidence of inattention or sleep rebound such as might have been exp ected.[22,71,72]

USWs in the cortex would be expected to save nearly one-half of the energy consumed by the forebrain that is saved during BSWS.[20,21] USWs are well suited to the dolphins' group activity patterns. Because dolphins and other cetaceans swim in pods, the visual world can be monitored by dolphins on each side of the pod and the remaining dolphins merely have to maintain contact with the pod. In routine "cruising" behavior this can be done with only one eye, allowing the other eye and connected portions of the brain to reduce activity as occurs in USWs. This hypothesis needs to be explored by EEG observations of groups of cetaceans in the wild.

In some smaller cetaceans, such as the harbor porpoise[73] and Commerson's dolphin,[74] motor activity is essentially continuous from birth to death; that is they never float or sink to the bottom and remain still. They move rapidly, and it is evident that they must have accurate sensory and motor performance and associated brain activation to avoid collisions. It is difficult to reconcile this behavior with the idea that all mammals "sleep" without discarding all aspects of the behavioral definition of sleep.[22] Put simply, we can say that Commerson's dolphin shows little or no sleep. Other small dolphins may share this behavioral pattern, as do all newborn dolphins and killer whales.

All studied land mammals have been reported to show maximal sleep and maximal immobility at birth, leading to the conclusion that sleep may be required for brain and body development. However, newborn killer whales and dolphins are continuously active for weeks to months after birth.[75] In captivity, they swim in tight formation and turn several times a minute to avoid conspecifics in the pool and pool walls. During this period the calves learn to nurse, breathe, and swim efficiently. Although some USWs might be present at these times, the eyes are open bilaterally when they surface at average intervals of less than 1 minute, indicating that any slow wave pattern could not last longer than this period.[75] Sleep interruption at such intervals can be lethal to rats,[76] and human sleep is not restorative if interrupted on such a schedule.[77] In the wild, mother and newborn calves migrate together, typically for thousands of miles from calving to feeding grounds. Sharks, killer whales, and other predatory animals target the migrating calves and a high level of continuous alertness is necessary for both mother and calf. Thus both cetaceans and migrating birds (see the section Sleep Rebound) greatly reduce sleep time during migrations without any sign of degradation of physiologic functions, sluggishness, loss of alertness, or impairment of cognitive function.

On land, sleep in the fur seal generally resembles that in most terrestrial mammals. The EEG is bilaterally synchronized, the animal closes both eyes, appears unresponsive, and cycles between REM and NREM sleep. In contrast, when the fur seal is in the water, it usually shows an asymmetric pattern of behavior, with one of the flippers being active in maintaining body position while the other flipper is inactive. During these periods, the fur seal has a high-voltage EEG with slow waves in one hemisphere with the contralateral eye generally closed. The other eye is generally open or partially open with an activated, waking-like EEG (Figure 10.6). Therefore unlike in the dolphin, it appears that half of the brain and body may in some sense be "asleep" and the other half "awake." Microdialysis studies showed that during asymmetric sleep, the waking hemisphere has significantly higher levels of acetylcholine release than the sleeping hemisphere.[78] In contrast, levels of serotonin,[79] histamine, and norepinephrine,[80] transmitters traditionally considered to be linked to arousal, do not differ between the hemisphere with high-voltage EEG and the hemisphere with low-voltage EEG.

When the fur seal goes into water, unihemispheric sleep occupies almost all of the sleep time and REM sleep virtually vanishes. When it returns to land there is no "rebound" of REM sleep.[81] Under natural conditions the fur seal spends at least 7 months of the year continuously at sea. The results in the fur seal reinforce the idea that the apparent absence of REM sleep in the dolphin is not a problem of the state being difficult to detect in cetaceans. Rather it appears that REM is linked to bilateral NREM sleep. In the absence of bilateral NREM, REM does not occur. I will deal with the issue of why this occurs, which bears directly on the issue of the function of REM sleep, in Chapter 8.

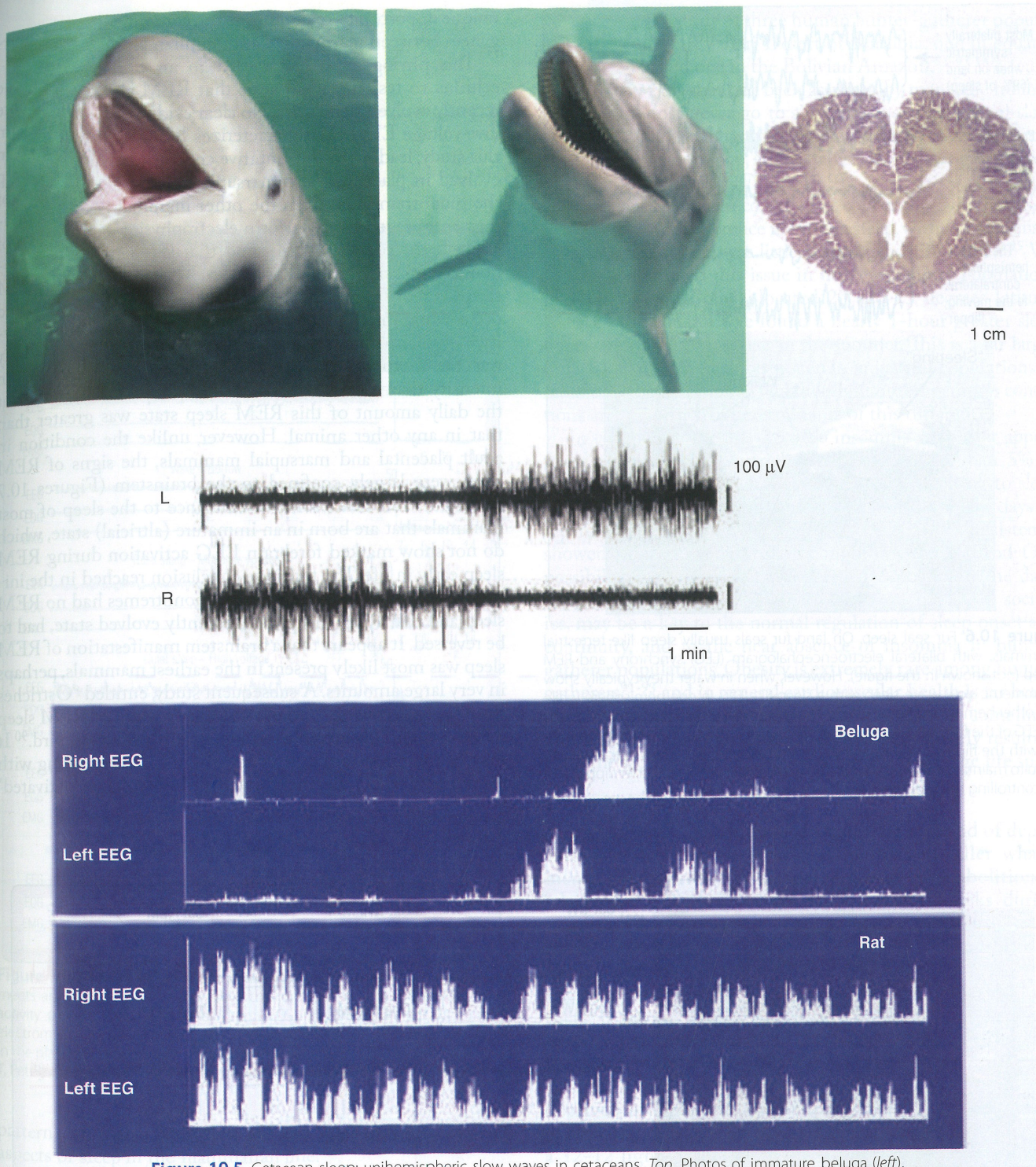

Figure 10.5 Cetacean sleep: unihemispheric slow waves in cetaceans. *Top*, Photos of immature beluga (*left*), adult dolphin and section of adult dolphin brain. Electroencephalogram (EEG) of adult cetaceans, represented here by the beluga, during sleep are shown. All species of cetacean so far recorded have unihemispheric slow waves. *Top traces* show left and right EEG activity. The spectral plots show 1-to 3-Hz power in the two hemispheres over a 12-hour period. The pattern in the cetaceans contrasts with the bilateral pattern of slow waves seen under normal conditions in all terrestrial mammals, represented here by the rat (*bottom traces*). (From Siegel JM. Clues to the functions of mammalian sleep. *Nature* 2005;437:1264–1271.)

Monotremes

The mammalian class can be subdivided into three subclasses: placentals, marsupials, and monotremes. There are just three extant monotreme species, the short-beaked and long-beaked echidna and the platypus. Fossil and genetic evidence indicates that the monotreme line diverged from the other mammalian lines about 150 million years ago and that both echidna species are derived from a platypus-like ancestor.[82-85] Although monotremes are distinctly mammalian, they do display a number of reptilian features, making study of their physiology a

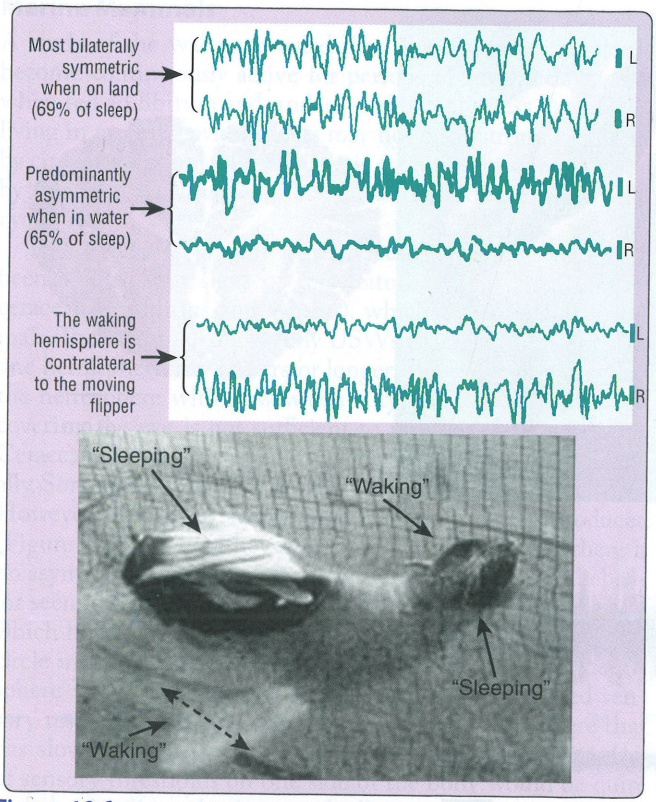

Figure 10.6 Fur seal sleep. On land fur seals usually sleep like terrestrial mammals, with bilateral electroencephalogram (EEG) synchrony and REM sleep (not shown in the figure). However, when in water they typically show asymmetric slow wave sleep with a sleep-like EEG in one hemisphere while the other hemisphere has a waking-like EEG. Unlike the dolphin, the asymmetric EEG of the fur seal is accompanied by asymmetric posture and motor activity with the flipper contralateral to the hemisphere with low-voltage activity used to maintain the animal's position in the water while the other flipper and its controlling hemisphere "sleep."

unique opportunity to determine the commonalties and divergences between mammalian and reptilian physiology.[83,86,87]

This phylogenetic history led to an early study of the echidna to test the hypothesis that REM sleep was a more recently evolved sleep state. No clear evidence of the forebrain low-voltage EEG that characterizes REM sleep was seen in this study, leading to the tentative conclusion that REM sleep evolved in placentals and marsupials after the divergence of the monotreme line from the other mammals.[88] These findings encouraged us to perform electrophysiological studies of sleep in the platypus. We found that the platypus had pronounced phasic motor activity typical of that seen in REM sleep[89] (see Video 10.1). This intense motor activity could occur while the forebrain EEG exhibited high-voltage activity,[36] similar to the phenomena seen in the echidna. Not only was the motor activity during sleep equal to or greater in intensity than that seen in REM sleep in other animals, but the daily amount of this REM sleep state was greater than that in any other animal. However, unlike the condition in adult placental and marsupial mammals, the signs of REM sleep were largely confined to the brainstem (Figures 10.7 and 10.8). This bears some resemblance to the sleep of most mammals that are born in an immature (altricial) state, which do not show marked forebrain EEG activation during REM sleep early in life. The tentative conclusion reached in the initial studies of the echidna, that the monotremes had no REM sleep and that REM sleep was a recently evolved state, had to be reversed. It appears that a brainstem manifestation of REM sleep was most likely present in the earliest mammals, perhaps in very large amounts. A subsequent study, entitled "Ostriches sleep like platypuses,"[90] found a similar pattern of REM sleep in the ostrich, considered to be a relatively "primitive" bird.[90] It may be the brainstem quiescence of NREM sleep along with the cortical EEG desynchrony (i.e., low-voltage "activated"

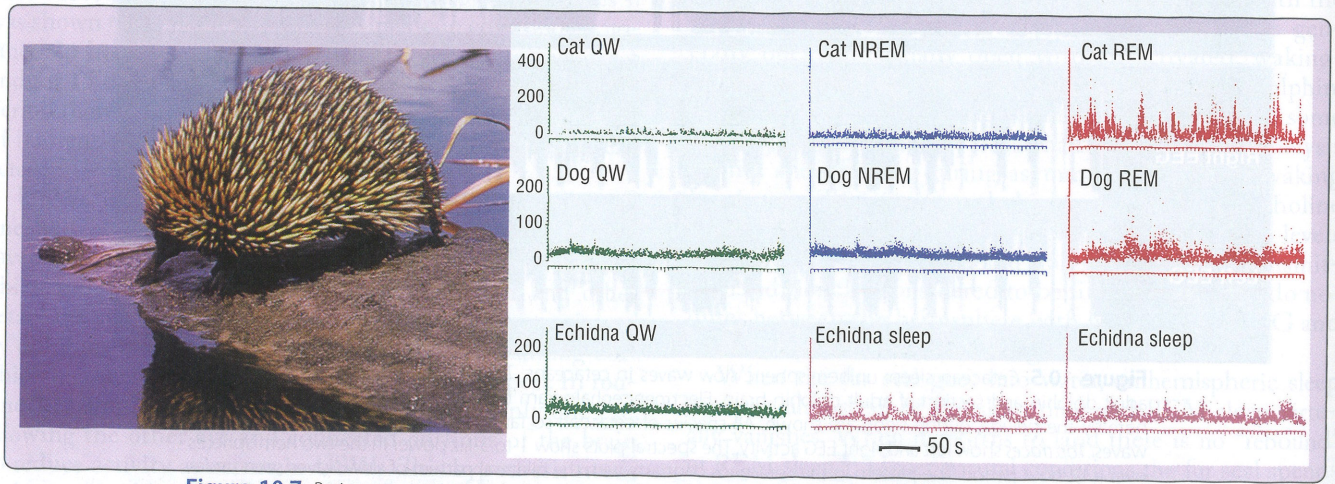

Figure 10.7 Brainstem activation during sleep in the echidna. Instantaneous compressed rate plots of representative units recorded in nucleus reticularis pontis oralis of the cat, dog, and echidna. Each point represents the discharge rate for the previous interspike interval. In cat quiet waking (QW) and NREM sleep, the discharge rate is low and relatively regular. The rate increases and becomes highly variable during REM sleep. A similar pattern can be seen in a unit recorded in the dog. In the echidna, sleep is characterized by variable unit discharge rates as is seen in REM sleep, but this occurs while the cortex is showing high-voltage activity. (From Siegel JM, Manger P, Nienhuis R, Fahringer HM, Pettigrew J. The echidna *Tachyglossus aculeatus* combines REM and nonREM aspects in a single sleep state: implications for the evolution of sleep. *J. Neurosci.* 1996;16:3500–3506.)

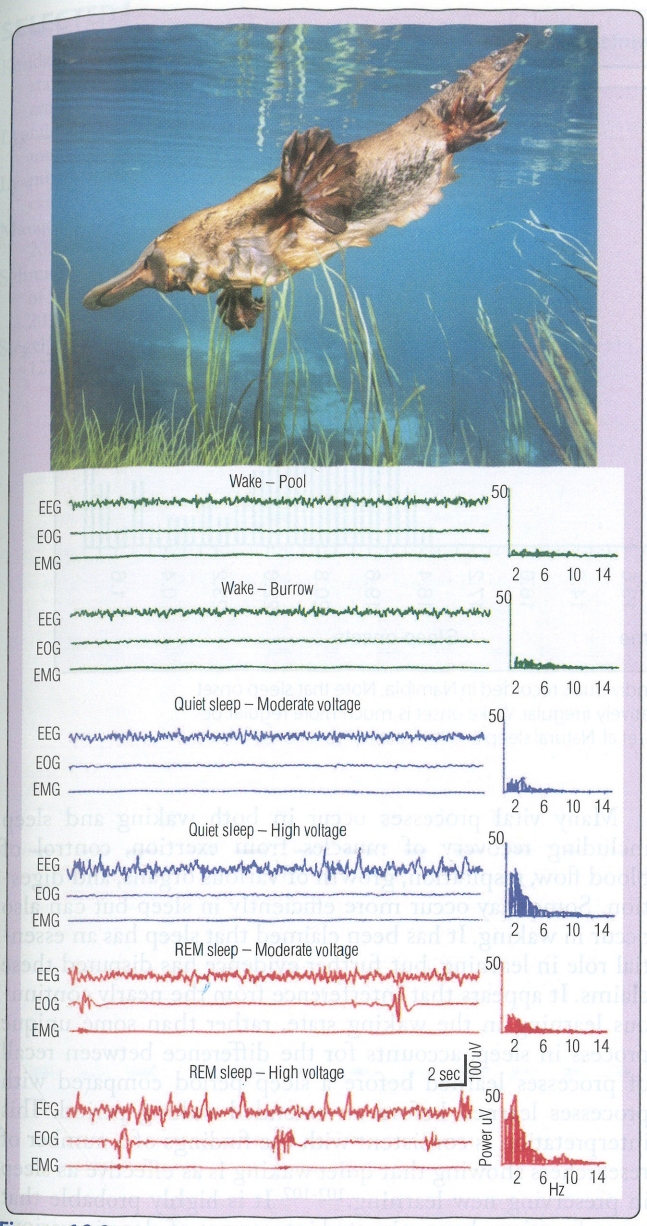

Figure 10.8 Brainstem REM sleep state in the platypus. Rapid eye movements and twitches can occur while the forebrain is showing a slow wave activity pattern. Electroencephalogram (EEG), electrooculogram (EOG), and electromyogram (EMG) power spectra of samples shown of sleep-wake states in the platypus. (From Siegel JM, Manger PR, Nienhuis R, Fahringer HM, Shalita T, Pettigrew JD. Sleep in the platypus. *Neuroscience* 1999;91:391-400.)

pattern) of REM sleep that are the most recently evolved aspects of sleep in the mammalian line.

Humans

The considerations reviewed earlier in this chapter and the great difference between sleep durations seen in elephants and sloths in captivity versus the same species "in the wild" made us wonder how humans slept before the industrial age. It has been commonly thought that electric lights have shortened sleep time in industrial populations and that this shortening may have had negative health consequences in humans. Therefore we undertook a study of three human hunter-gatherer populations, one in the Kalahari Desert of Namibia, one in equatorial Tanzania, and one in the Bolivian Amazon.[91-93] We found that, contrary to what had been assumed by many, the hunter-gatherers almost never go to sleep at sunset, have total sleep durations that are somewhat shorter than those in industrial populations, seldom nap, and usually sleep in a single uninterrupted nightly block[92] (Figure 10.9).

There has long been controversy concerning whether there was any seasonal difference in human sleep, with the consensus view being that here was little if any such difference.[94,95] We therefore examined this issue in hunter-gatherer populations in Namibia and Bolivia, located 20 and 15 degrees latitude south of the equator. We found a nearly 1-hour greater sleep duration in the winter than in the summer. This is a far larger difference than has ever been seen in industrial populations. It remains to be determined whether light or temperature conditions are the principal determinants of this difference.

In contrast to the 10% to 30% insomnia rates that appear to be universal in industrial populations, fewer than 5% of hunter-gatherers report having any difficulty getting to sleep or staying asleep. Similarly, in our more than 1165 days of recording we did not see any individuals who consistently showed reduced sleep during the nighttime sleep period. One possibility we are investigating is that exposure to the daily temperature rhythm, largely eliminated in industrial societies, may be a key to the normal regulation of sleep onset and continuity, and to the near absence of insomnia in hunter-gatherer populations. Obesity is extremely rare among hunter-gatherers[91-93] and in general cardiovascular health is far better than in industrial populations.[96] This reality is sometimes obfuscated by the high childhood death rate, largely resulting from the lack of vaccinations, which reduces average life span.

Sleep Rebound

Sleep rebound,[97] the increased sleep after a period of deprivation, is not always seen. In dolphins and killer whales mentioned earlier in this chapter, a near total abolition of "sleep-like behavior" for periods of several weeks during migration is followed by a slow increase back to baseline levels with no rebound above baseline. The same phenomenon is seen in migrating white sparrows.[98] Humans with mania greatly reduce sleep time for extended periods and there is no persuasive evidence for progressive degradation of performance or physiologic function during the manic period, despite the emotional pathology, or of sleep rebound after this period. Zebrafish can be completely deprived of sleep for an extended period by placing them in continuous light but show no rebound when returned to a 12-12 light-dark cycle.[99] On the other hand, when they are deprived by repetitive tactile stimulation they do show rebound, suggesting that the deprivation procedure, rather than the sleep loss, underlies the rebound. Stressing rats by restraint can produce increased REM sleep even when no sleep has been lost. This is mediated by the release of pituitary hormones.[100,101] It is possible that in some species other aspects of rebound are driven by changes in hormonal release linked to sleep deprivation[1] rather than by some intrinsic property of sleep.

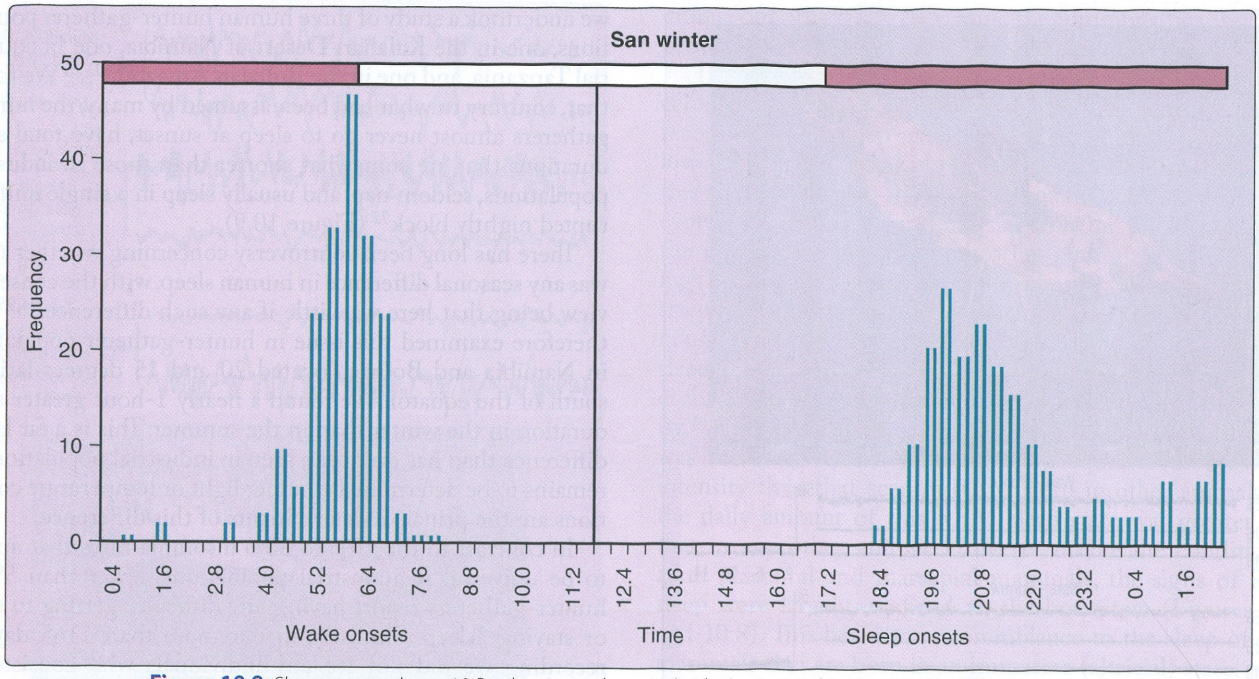

Figure 10.9 Sleep averaged over 10 San hunter-gatherer individuals recorded in Namibia. Note that sleep onset occurs on average more than 3 hours after sunset and is relatively irregular. Wake onset is much more regular occurring before and after dawn. (Yetish, G, Kaplan H, Gurven M, et al. Natural sleep and its seasonal variations in three pre-industrial societies. *Curr Biol.* 2015;25(21):2862–2868.)

CLINICAL PEARL

Although sleep and sleep stages differ in amount between species, human sleep does not appear to be qualitatively unique. This factor makes animal models suitable for the investigation of many aspects of pharmacology and pathology.

SUMMARY

Sleep can be seen as an adaptive state, benefiting animals by increasing the efficiency of their activity. Sleep does this by suppressing activity at times that have maximal predator risk and permitting activity at times of maximal food and prey availability. It also increases efficiency by decreasing brain and body metabolism. However, unlike the dormant states employed in plants, simple multicellular organisms, and ectothermic organisms and the hibernation and torpor employed in some mammals and birds, sleep allows rapid arousal for tending to infants and responding to environmental changes. Many organisms can reduce sleep for long periods of time without rebound during periods of migration.

The big brown bat, currently documented as having the longest sleep time of any mammal, specializes in eating mosquitoes and moths that are active from dusk to early evening. The big brown bat typically is awake only about 4 hours a day.[29] This waking is synchronized to the period when flies are active. It is not likely that this short waking period can be best explained by the need for some time-consuming unknown process that occurs only during sleep and requires 20 hours to complete. It can be more easily explained by the ecological specializations of this bat. Similarly "sleep" in ectothermic animals is most likely determined by temperature and other environmental variables, rather than any information processing or physiologic maintenance requirement.

Many vital processes occur in both waking and sleep including recovery of muscles from exertion, control of blood flow, respiration, growth of various organs, and digestion. Some may occur more efficiently in sleep but can also occur in waking. It has been claimed that sleep has an essential role in learning, but further evidence has disputed these claims. It appears that interference from the nearly continuous learning in the waking state, rather than some unique process in sleep, accounts for the difference between recall of processes learned before a sleep period compared with processes learned before an extended waking period. This interpretation is consistent with the findings of a number of researchers showing that quiet waking is as effective as sleep in preserving new learning.[102-107] It is highly probable that some functions have migrated into or out of sleep in various animals. Neurogenesis,[106] synaptic downscaling,[107] immune system activation, and reversal of oxidative stress may be accomplished in sleep in mammals. It remains to be seen if these or any other vital functions can be performed only in sleep. However, this review of the phylogenetic literature suggests that such functions cannot explain the variation of sleep amounts and the evident flexibility of sleep physiology within and between animals. Viewing sleep as a period of well-timed adaptive inactivity that regulates behavior and reduces energy consumption, can better explain this variation.

ACKNOWLEDGMENTS

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See discussion of the evolution and diversity of sleep at http://thesciencenetwork.org/programs/sleep-2009/jerome-siegel.

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