Sleep in Animals: A State of Adaptive Inactivity

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Abstract

In most adult animals sleep is incompatible with mating and feeding. Animals are believed to be vulnerable to predation during sleep. Humans frequently see sleep as an obstacle to a productive life. Many people use alarm clocks to truncate sleep and take stimulants, such as caffeine, to maintain alertness after insufficient sleep. Why do animals devote from 2 to 20 hours of the day to sleep, in what appears to be a nonproductive state? Why has evolution preserved this state? It is often said that sleep must have some unknown vital function to have persisted in all humans and throughout much, though not necessarily all,[1] of the animal kingdom. Without this so far undiscovered function, it has been said that sleep would be evolution's greatest mistake.

Sleep is not a maladaptive state that needs to be explained by undiscovered functions (which nevertheless undoubtedly exist). Rather, the major function of sleep is to increase behavioral efficiency. Greater waking activity does not necessarily lead to increased numbers of viable offspring and, hence, genetic success. Rather, genetic success is closely linked to the efficient use of resources and to the avoidance of risk. Thus, inactivity can reduce predation and injury. It also reduces brain and body energy consumption. It has often been stated that energy conservation is not a sufficient explanation for sleep because the energy saved in a night's sleep in humans is only equivalent to that contained in a slice of bread, although to the extent that sleep prevents locomotor activity the energy savings are much greater. In the wild, most animals are hungry and are seeking food most of the time they are awake. The ability of sleep to conserve energy when food is scarce will produce a major survival benefit. Conversely, if food is available but is time consuming to acquire, then it is highly advantageous for animals to be able to reduce sleep time without behavioral impairment.[2] Similarly, it is highly advantageous to reduce or eliminate sleep to allow migration and to respond to certain other needs.

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.[1] 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, making it difficult to see how they would get the unknown benefit that sleep supposedly confers. 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.[3]

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 it continues to be essential for the preservation of many organisms. Many species have evolved seasonal dormancy patterns that allow them to anticipate periods that are not optimal for survival and propagation (predictive dormancy). In other species dormancy is triggered by environmental conditions (consequential dormancy). Many organisms spend most of their lifespan in dormancy. A continuum of states of adaptive inactivity can be seen in living organisms including plants, unicellular and multicellular animals, and animals with and without nervous systems.[3a]

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 1300 years of dormancy.[4] More recently it was found that a seed from a 2000-year-old palm tree seed produced a viable sapling. http://news.nationalgeographic.com/news/2005/11/1122_051122_old_seed.html. Some forms of vegetation can germinate only after fires that may come decades apart. These include the giant sequoias native to the southwest United States as well as many other species of trees and grass. Most decidu-

ous trees and plants have seasonal periods of dormancy during which they cease photosynthesis, a process called abscission. These periods of dormancy enhance plant survival by synchronizing growth to optimal conditions. Clearly this mechanism has evolved to time germination to optimal conditions, that is, not in a dry clay pot or when growth conditions will not be optimal for survival. Energy savings is not the only reason for dormancy in plants or animals.

Many unicellular organisms (protozoans) have evolved to live in environments that can only sustain them for portions of the year because of changes in temperature, water availability or other factors. Their survival requires that they enter dormant states that can be reversed when optimal conditions reappear.

A tiny colony of yeast trapped inside a Lebanese weevil covered in ancient Burmese amber for up to 45 million years has been brought back to life and used to brew a modern beer (http://www.foodinthefort.com/tag/raul-cano/). Rotifers, a group of small multicellular organisms of microscopic or submicroscopic size (up to 0.5 mm long) 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 also have extended dormant periods, defending themselves by forming a protective cyst.[8] In some cases the cyst can only be dissolved and the parasite activated by digestive juices. Many sponges have a similar dormant state which allows

them to survive suboptimal conditions by being encased in "gemmules."

Insect dormancy or diapause can be seasonal lasting several months, and anecdotal reports indicate that it, 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. In a few cases insects have evolved a vibrational defensive response which is elicited when pupae are disturbed. Land snails and slugs can secrete a mucus membrane for protection and enter a dormant state when conditions are not optimal.[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 (called brumination in reptiles). These dormant periods may occur just during the cool portion of the circadian cycle or may extend for months in winter.[11]

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, sleep periods. During hibernation, body temperature can be reduced to below 10°C to as low as −3°C with greatly reduced energy consumption.[12,13] Animals are quite difficult to arouse during hibernation, with arousal taking many minutes. Consequently, hibernators are vulnerable to predation and survive hibernation by seeking protected sites. Torpor[12] is another form of dormancy which can be entered by mammals and birds daily. Torpor is entered and exited through 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,[14] 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 previously. 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.[14a,15,16]

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 food needs of the family.

The continuum from adaptive inactivity to high levels of activity can be seen within the life cycle of some animals. Thus, some animals that live in climates with a pronounced seasonal reduction in food or light availability or a periodic increase in threat from predators may need to migrate to survive. Many species of birds do this as do certain species of marine mammals (discussed later). Although some may maintain circadian rhythms of activity during migration, others remain continuously active for weeks or months. Some vertebrate species do not ever appear to meet the behavioral criteria for sleep, remaining responsive, or responsive and active, throughout their lifetime.[1]

Humans with insomnia, who are typically not sleepy during the day despite reduced sleep at night, 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.[17] Individuals with restless legs syndrome are similarly unlikely to be sleepy during the day despite low levels of nightly sleep. Conversely, many individuals with hypersomnia appear to need more sleep and sleep more deeply, rather than being the victims of shallow or disrupted sleep that is compensated for by extended sleep time.

To summarize, evolution has produced a wide range of forms of diurnal or seasonal adaptive inactivity, some of which are accompanied by a virtual cessation of metabolism and responsiveness. Clearly, evolution rewards judicious activity, not continuous activity. Sleep is often viewed as a liability because of its reduced alertness compared to quiet waking. However, seen in the context of adaptive inactivity shown by most species, what is most notable about sleep in humans is its intermediate status, between the highly inactive unresponsive states seen in rotifers, insects, and hibernating mammals (which show little neuronal activity during hibernation), and the virtually continuous periods of activity and waking that have been seen in migrating birds and cetaceans.

QUANTITATIVE ANALYSES OF THE CORRELATES OF SLEEP DURATION

An increasing number of studies have attempted to correlate the data that has been collected on sleep duration in mammals with a number of physiological and behavioral variables in order to develop hypotheses as to the function of sleep. The data these studies are based on are not ideal. Only approximately 60 mammalian species have been studied with sufficient measurements to determine the amounts of rapid eye movement (REM) and non-REM (NREM) sleep over the 24-hour period. These species are by no means a random sample of the more than 5,000 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* and are on artificial light cycles at thermoneutral temperatures. These environments differ greatly from

those in which they evolved. Digital recording and storage technologies now exist that will enable the collection of polygraphic data on animals in their natural environment[18] but they have not yet been widely used. Such observations are necessary to determine the variation in sleep times caused by hunger, response to temperature changes, predation and other variables that have driven evolution. Very few of these animals have been tested for arousal threshold, the nature and extent of sleep rebound, and other aspects of sleep whose variation across species might contribute to an understanding of sleep evolution and function. An important issue in comparing sleep times in animals is determining sleep depth. In humans we know that sleep depth, as assessed by either arousal threshold or electroencephalogram (EEG) amplitude, increases after sleep deprivation and is often greater during early stages of development when total sleep time is greatest. Can sleep time be profitably compared across animals without incorporating information on sleep depth? Should we assume that animals that sleep for longer periods also sleep more deeply as is true across human development, or should we assume the reverse, that short sleeping animals sleep more deeply as has been hypothesized?[19]

One of the earliest studies comparing REM and NREM sleep durations with physiological variables, found that sleep duration was inversely correlated with body mass.[20,21] A subsequent analysis found that this relationship applied only to herbivores, not to carnivores or omnivores.[3] This study also showed that, as a group, carnivores slept more than omnivores, who in turn slept more than herbivores (Fig. 10-1). Significant negative correlations were found between brain weight and REM sleep time (but not total sleep time). It should be emphasized that this latter correlation was extremely small, accounting for only 4% of the variance in REM sleep time between species (Fig. 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 time is about 10 minutes in mice, 90 minutes in humans, and 2 hours in elephants. Another robust correlation in the Zepelin study was between adult REM sleep time and immaturity at birth, that is, animals that are born in a relatively helpless state have greater amounts of REM sleep as adults than animals born in a more mature state. Because sleep is linked to a reduction in body temperature[22] and a reduction in energy usage, it has been hypothesized that energy conservation may be a function of sleep.[23]

Several studies have reanalyzed the phylogenetic data set with the addition of the few more recently studied animals. These studies took a variety of strategies to extract relations from this data set. Lesku et al.[24] used a method of "independent contrasts" in an attempt to control for the relatedness of species being compared. 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 recent 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,[25] in contrast to earlier studies.[21] This result is not inconsistent with some prior work.[3] They also reported that neither adult nor neonatal brain mass correlates positively with adult REM or NREM sleep times, differing from earlier studies.[21,25] They find, in agreement with prior analyses, that animals with high predation risk sleep less.[3,26] 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.

A notable feature of the Lesku et al. study and the Capellini et al. studies is that both excluded animals that they decided had unusual sleep patterns. So the echidna, which combines REM and NREM features in its sleep[27] was eliminated from the analysis. The platypus, which has the largest amount of REM sleep of any animal yet studied[28] was also excluded from this analysis as it was from another study focusing on brain size relations.[29] The dolphin and three other cetacean species and two species of manatee were excluded from the Lesku et al. study because of their low levels of REM sleep and unihemispheric slow waves. Including these species in their analyses would undoubtedly negate or reverse the positive relationship they report between brain size and REM sleep, because 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 little or no REM sleep, has a larger brain size than humans. As I will discuss hereafter, these "unusual" species that have been excluded from prior analyses may in fact hold the most 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. A recent correlational analysis of sleep parameters in birds, which paralleled the studies done in mammals, found no relationship between brain mass, metabolic rate, relative metabolic rate, maturity at birth and total sleep time or REM sleep time.[30] All values for 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 previously 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 reach disparate and often opposite conclusions about the physiological 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 as currently used is getting at the core
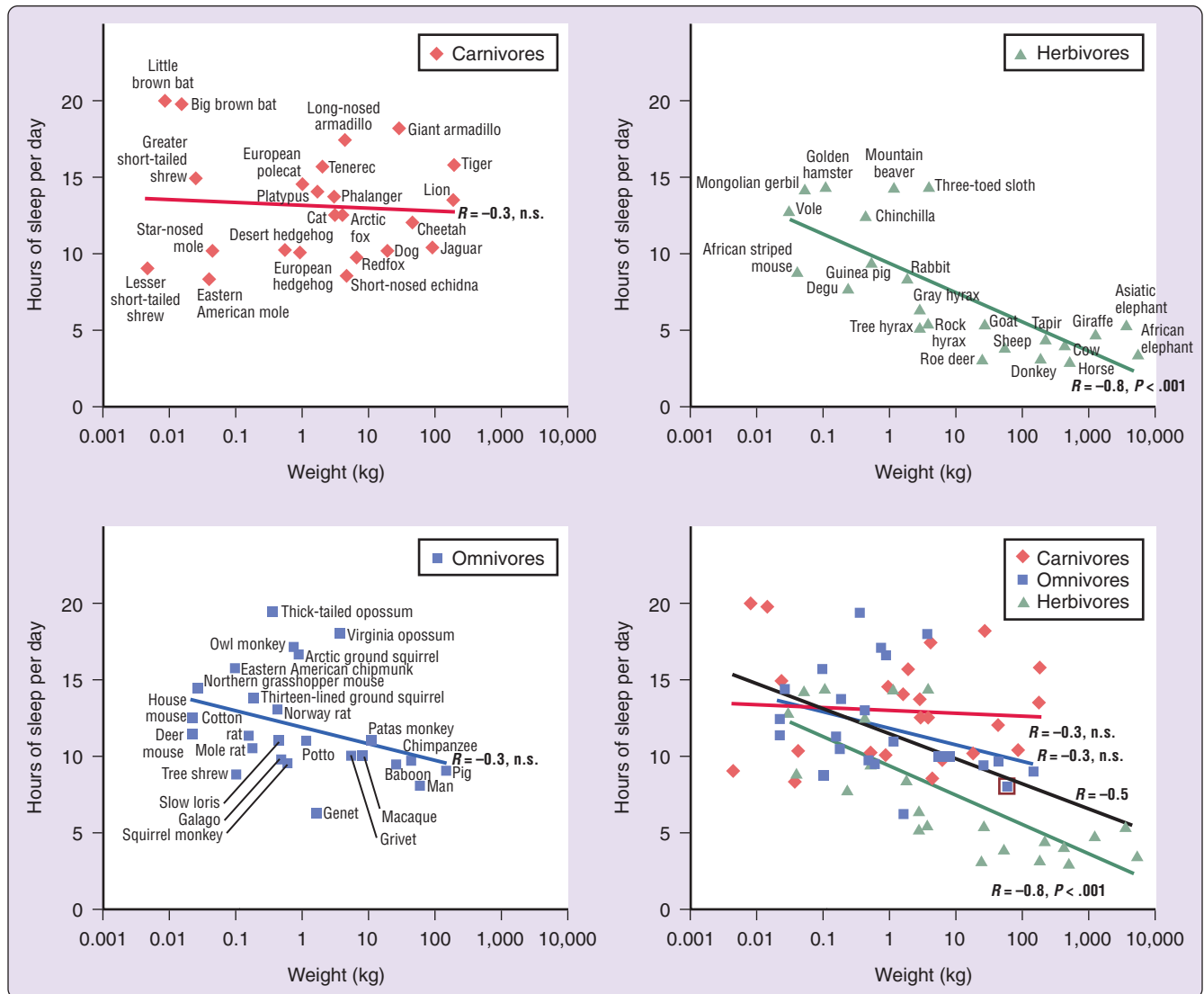
Figure 10-1 Sleep time in mammals. **A**, Carnivores are shown in dark red; **B**, herbivores are in green and **C**, omnivores in grey. Sleep times in carnivores, omnivores and herbivores differ significantly, with carnivore sleep amounts significantly greater than those of herbivores. Sleep amount 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. Small red box in the combined figure (lower right) indicates human data point. (From Siegel JM. Clues to the function of mammalian sleep. Nature 2005;437:1264-1271.)
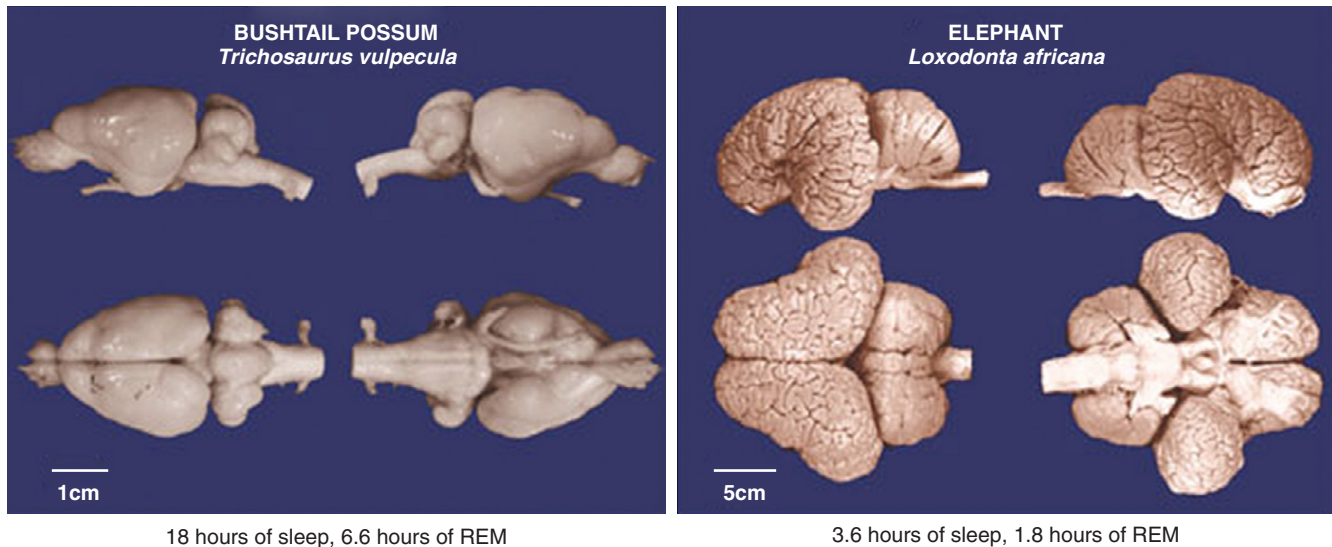
issues of sleep function. Despite similar genetics, anatomy, cognitive abilities and physiological functioning, closely related species can have very different sleep parameters and distantly related species can have very similar sleep parameters. Many such examples exist despite the relatively small number of species in which REM and NREM sleep time have been determined (Fig. 10-3).

THE DIVERSITY OF SLEEP

On the assumption that sleep satisfies an unknown, yet universal function in all animals, recent work has been carried out on animals whose genetics and neuroanatomy is better understood and more easily manipulated than that 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 thresh-

old is elevated during periods of immobility but 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 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. Octopamine, a major sleep regulating transmitter in drosophila does not exist in mammals. Hypocretin, a major sleep regulating transmitter in mammals does not exist in *Drosophila*.[31] *Drosophila* are not homeotherms, whereas thermoregulation has been closely linked to fundamental aspects of mammalian sleep.[3,22,32] There is no evidence for the occurrence of a state resembling REM sleep in *Drosophila*. Thus the neurochemistry, neuroanatomy, and neurophysiology of sleep must necessarily differ

BUSHTAIL POSSUM *Trichosaurus vulpecula*	ELEPHANT *Loxodonta africana*
1cm	5cm
18 hours of sleep, 6.6 hours of REM	3.6 hours of sleep, 1.8 hours of REM

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 function of mammalian sleep. Nature 2005;437:1264-1271.)

among *Drosophila*, man, and other mammals. Any commonality of sleep phenomena would have to be restricted to cellular level processes. Two recent studies have shown that drosophila sleep and sleep rebound is markedly impaired by genetic alteration of a potassium current that regulates neuronal membrane excitability.[33,34] Regulation of potassium currents may be a core function of sleep or it may instead affect the excitability of circuits regulating activity and quiescence, just as such currents affect seizure susceptibility.[35,36]

Caenorhabditis elegans, a roundworm with a nervous system much simpler than that of *Drosophila*, has also been investigated for sleeplike behavior.[37] *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 prior to 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* show any aspect of sleep behavior.[38]

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, and cats, the most studied species.[39-41] Human stage 4 NREM sleep is linked to growth hormone secretion. Disruption of stage 4 sleep in children is thought to cause short stature. However, in dogs, growth hormone secretion normally occurs in waking, not sleep.[42] Melatonin release is maximal during sleep in diurnal animals, but is maximal in waking in nocturnal animals.[43] Erections have been shown to be present during REM sleep in humans and rats,[44] however the armadillo has erections only in NREM sleep.[45] Blood flow and metabolism differ dramatically between neocortical regions in adult human REM sleep,[46] although most animal sleep deprivation and

sleep metabolic studies treat the neocortex as a unit. Lesions of parietal cortex and certain other regions prevent dreaming in humans, even in individuals continuing to show normal REM sleep as judged by cortical EEG, rapid eye movements and suppression of muscle tone.[47] Humans before age 6 do not have dream mentation, perhaps because these cortical regions have not yet developed.[48] 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.

SLEEP IN 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 (Video 10-1). 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.[49-52] The monotremes have shown a remarkably conservative evolutionary course since their divergence from the two other mammalian lines. For example, fossil teeth from *Steropodon galmani* dated at 110 million years ago show many similarities to the vestigial teeth of the current day platypus, *Ornithorhyncus anatinus*.[53] Analyses of fossilized skull remains indicate remarkably little change in platypus morphology over at least 60 million years.[53,54] The low level of speciation throughout the fossil record is another indicator of the uniquely conservative lineage of monotremes. The 150 million years of platypus evolution has produced no species radiation, apart from the echidna line, and there are only two living and one extinct species of echidna. Although monotremes are distinctly mammalian, they do display a number of reptilian features, making study of their physiology a unique opportunity to determine the commonalities and divergences in mammalian evolution.[50,55,56]

Figure 10-3 Mammalian phylogenetic order is not strongly correlated with sleep parameters. Despite similar genetics and physiology, sleep times within mammalian orders overlap extensively. 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.)

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 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.[57] We reexamined this issue using single neuron recording techniques, in addition to the EEG measures employed in the prior studies. REM sleep is generated in the mesopontine brainstem (see Chapter 8) and is characterized by highly variable burst pause

activity of brainstem neurons. This activity is responsible for driving the rapid eye movements, twitches, and other aspects of the REM sleep. We recorded from these brainstem regions in unrestrained echidnas to see if this activation was absent throughout sleep. We found that instead of the slow, regular activity that characterizes brainstem neurons in many nuclei during NREM sleep in placental mammals,[58,59] the echidna showed the irregular activity pattern of REM sleep throughout most of the sleep period (Fig. 10-4).[27,60] It appeared that the brainstem was in an REM sleeplike state, whereas the forebrain was in an NREM sleep state. Other investigators
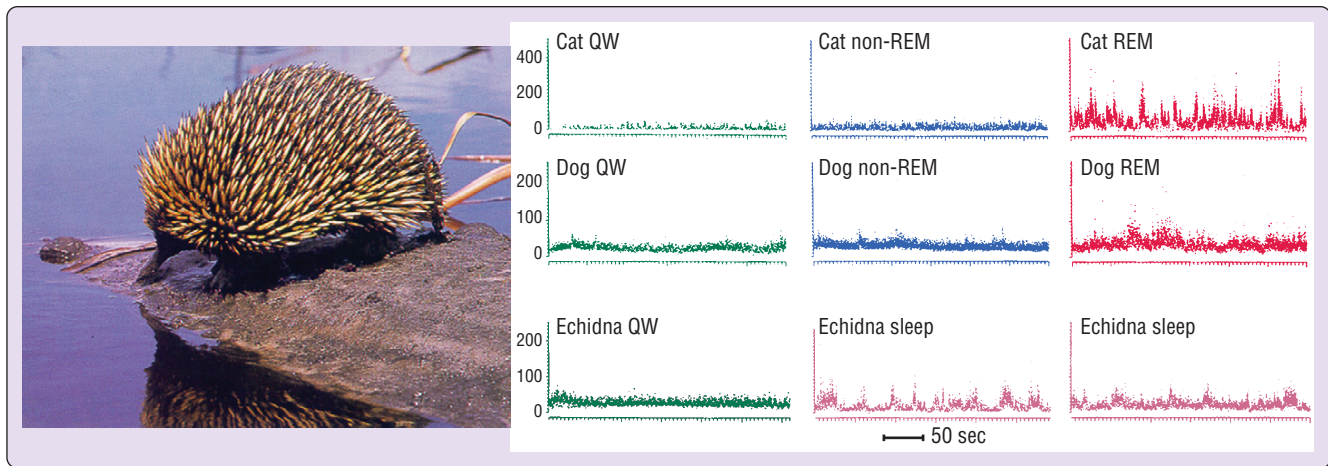
Figure 10-4 Brainstem activation during sleep in the echidna. Instantaneous compressed rate plots of representative units recorded in nucleus reticularis pontis oralis of the cat, dog, and echidna. Each point represents the discharge rate for the previous interspike interval. In cat QW and non-REM sleep, 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 PR, Nienhuis R, et al. The echidna *Tachyglossus aculeatus* combines REM and non-REM aspects in a single sleep state: implications for the evolution of sleep. J Neurosci 1996;16:3500-3506.)

also concluded that the echidna had an REM sleeplike state.[61]

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 (see video on PPSM web-site and at http://www.npi.ucla.edu/sleepresearch/media.php). This intense motor activity could occur while the forebrain EEG exhibited high-voltage activity,[28] 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 also 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 (Fig. 10-5). This bears some resemblance to the conditions in 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. It may be the brainstem quiescence of NREM sleep, and likely reduction in brain energy consumption that is the most recently evolved aspect of sleep in the mammalian line.

REINDEER

Reindeer are ruminants. Like other ruminants they appear to remain active over the entire circadian cycle to an extent not seen in most carnivores and omnivores. A recent study examined the activity of two species of reindeer living in polar regions where they experience periods of continuous darkness in the winter and continuous light in the summer. Activity was monitored for an entire year. This was the

first such study and contrasts with the constant conditions of light and temperature usually employed in laboratory studies. It was found that the circadian rhythm of melatonin and circadian rhythms of behavioral activity dissipated in winter and summer. It was also reported that activity time was from 22% to 43% greater in summer than in winter (calculated from Figure 4 in van Oort and Tyler[62]).[63] EEG recording and arousal threshold tests were not done, however, the activity changes suggest that major changes in sleep duration occur seasonally.

BIRDS

Birds have REM sleep that appears physiologically very similar to that seen in mammals, although REM sleep values tend to be lower in comparison to total sleep values than in mammals.[30] Many bird species migrate over long distances. The effect of this migratory behavior on sleep has been studied in the white-crowned sparrow (*Zonotrichia leucophrys gambelii*). These birds, even when confined in the laboratory, decrease sleep time by two thirds during the periods when they would normally be migrating.[64] It should be noted that this is a common feature of cycles of adaptive inactivity; for example, a ground squirrel that normally hibernates in the winter will enter a state of torpor at the appropriate season even when maintained in a laboratory under constant conditions.[65]

During the migratory period, the sparrow's learning and responding was unimpaired or improved. Their sleep was not deeper by EEG criteria than that seen when they were not migrating, despite its greatly reduced duration. Their sleep latency did not differ from that during nonmigrating periods.[64]

The observations in monotremes and birds suggest that the reptilian common ancestor of both mammals and birds had REM sleep or a closely related precursor state, rather than the previously advanced speculation that REM sleep must have evolved twice based on the prior conclusion that monotremes did not have REM sleep. Although there
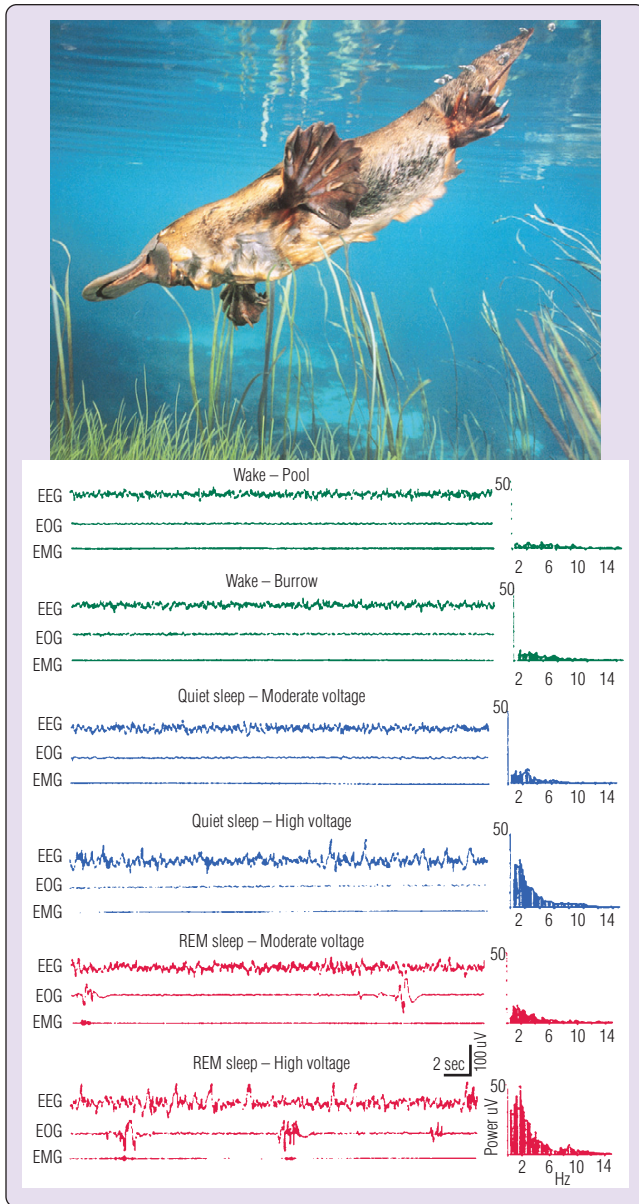
Figure 10-5 Brainstem REM sleep state in the platypus. Rapid eye movements and twitches can occur while the forebrain is showing a slow-wave activity pattern. EEG, EOG, EMG and EEG power spectra of samples shown of sleep–wake states in the platypus. (From Siegel JM, Manger PR, Nienhuis R, Fahringer HM, et al. Sleep in the platypus. Neuroscience 1999; 91:391-400.)

were scattered early reports claiming to have seen REM sleep in reptiles, these have not been replicated.[3] We applied the same recording techniques we had used in the echidna to the turtle in a search for evidence of REM sleep. We saw no evidence of phasic brainstem neuronal activity during quiescent states in this reptile.[66]

WALRUS

A recent 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.[67] Such behaviors have not been reported in terrestrial mammals, although they cannot be ruled out. 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.

SLEEP IN CETACEANS (DOLPHINS AND WHALES)

REM sleep is present in all terrestrial animals that have been studied, but signs of this state have not been seen in cetaceans, which are placental mammals. These animals show only unihemispheric slow waves (USW), which 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 in the contralateral hemisphere.[28,68] They never show persistent high voltage waves bilaterally. Sometimes they float at the surface while showing USW. However, often they swim while USW are being produced (Fig. 10-6). When they swim while having USW, there is no asymmetry in their motor activity, in contrast to the behavior seen in the fur seal. Regardless of which hemisphere is showing slow wave activity, they tend to circle in a counterclockwise direction (in the northern hemisphere[69]). 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. Therefore, forebrain and brainstem sensory and motor activity must differ radically during USW from that seen in terrestrial mammals during sleep (see Chapter 8).[58,59] 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 another study it was shown that dolphins are able to maintain continuous vigilance for 5 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 would be expected of a sleep deprived animal.[1,71]

Unihemispheric slow waves would be expected to save nearly one half of the energy consumed by the brain that is saved during bilateral slow wave sleep (BSWS).[15,16] Unihemispheric slow waves 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 USW. This hypothesis needs to be explored by electroencephalographic observations of groups of cetaceans in the wild.

In some smaller cetaceans, such as the harbor porpoise[72] and Commerson's dolphin,[73] 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
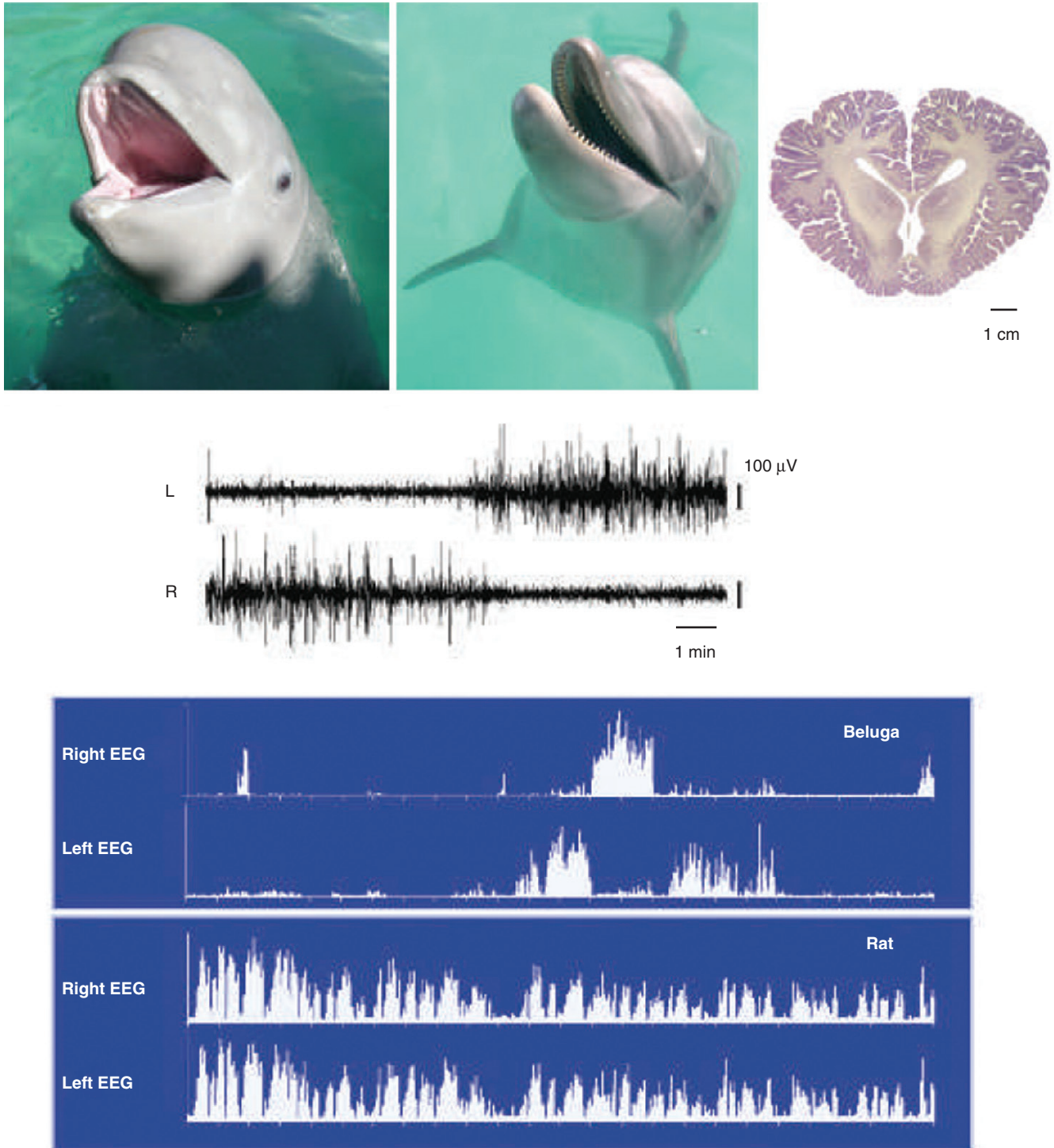
Figure 10-6 Cetacean sleep, unihemispheric slow waves in cetaceans. *Top*, photos of immature beluga, adult dolphin and section of adult dolphin brain. Electroencephalogram (EEG) of adult cetaceans, represented here by the beluga, during sleep are shown. All species of cetacean so far recorded have unihemispheric 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 function of mammalian sleep [review]. Nature 2005;437:1264-1271.)

it is evident that they must have accurate sensory and motor performance and associated brain activation to avoid collisions. It is difficult to accept this behavior as "sleep" without discarding all aspects of the behavioral definition of sleep.[1]

All studied land mammals have been reported to show maximal sleep and maximal immobility at birth, leading to the conclusion that sleep is required for brain and body development. However, newborn killer whales and dolphins are continuously active. 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.[74] Sleep interruption at such intervals can be lethal to rats,[75] and human sleep is not restorative if interrupted on such a schedule.[76] The cetacean mothers also cease eye closure at the surface and floating behavior and are continuously active during the postpartum period. No loss of alertness is apparent during the "migratory" period. In the wild, mother and calf 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 during migration. One could describe the maternal and neonatal pattern as "sleep" with well coordinated motor activity, accurate sensory processing, effective response to threats in the environment, and without the likelihood of any EEG slow waves or eye closure lasting more than 60 seconds.[77,78] However, this does not comport with the accepted behavioral definition of sleep.[79] Thus both cetaceans and migrating birds greatly reduce sleep time during migrations without any sign of degradation of physiological functions, sluggishness, loss of alertness, or impairment of cognitive function.

SLEEP IN OTARIIDS (EARED SEALS)

On land, sleep in the fur seal generally resembles that in most terrestrial mammals. The EEG is bilaterally synchronized and 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 asymmetrical pattern of behavior with one of the flippers being active in maintaining body position, while the other flipper is inactive. The fur seal can have slow waves in one hemisphere with the contralateral eye being closed. The other eye is generally open or partially open (Fig. 10-7). Therefore, it appears that half of the brain and body may be "asleep" and the other half "awake." A microdialysis study showed that during asymmetrical sleep, the waking hemisphere has significantly higher levels of acetylcholine release than the sleeping hemisphere.[80]

SLEEP REBOUND

Sleep rebound is not always seen. When the fur seal goes in the water for extended periods, as they do in winter, REM sleep time is greatly reduced. There is little or no rebound of lost REM sleep when the fur seal returns to land, even after several weeks in the water.[81] In the cases of the dolphins and killer whales mentioned previously, a near total abolition of sleep for periods of several weeks during migration is followed by a slow increase back to baseline levels with no rebound. The same phenomenon is seen in migrating white sparrows, a species that has been carefully studied under laboratory conditions.[64] Manic humans greatly reduce sleep time for extended periods, and there is no persuasive evidence for progressive degra-
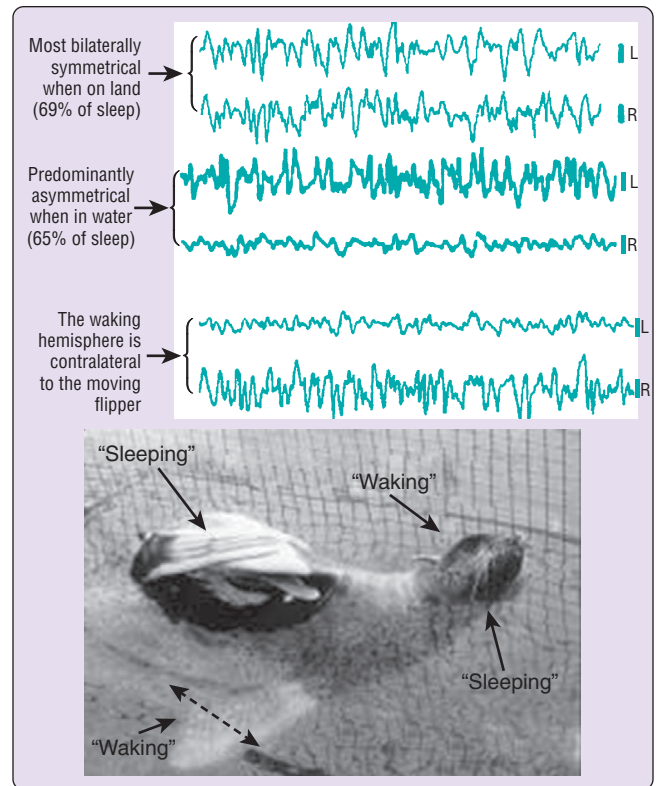
Figure 10-7 Fur seal sleep. On land fur seals usually sleep like terrestrial mammals, with bilateral EEG synchrony and REM sleep (not shown in the figure). However, when in water they typically show asymmetrical slow-wave sleep, with a sleeplike EEG in one hemisphere while the other hemisphere has a waking-like EEG. Unlike the dolphin, the asymmetrical EEG of the fur seal is accompanied by asymmetrical 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."

dation of performance, physiological function, or sleep rebound during this period. Zebrafish can be completely deprived of sleep for three days by placing them in continuous light, but show no rebound when returned to a 12-12 light–dark cycle.[82] On the other hand, when they are deprived by repetitive tactile stimulation they do show rebound.

Typically 30% or less of lost sleep is recovered in the human and rodent studies, in which the phenomenon has been most extensively studied. A similar percent of rebound is seen in other species including some invertebrates (see Chapter 9). One may ask why, if sleep is essentially a maladaptive state, animals that have the ability to regain lost sleep in 30% of the time it would normally have taken have not evolved shorter sleep times to take advantage of the adaptive benefits of increased waking. However, if sleep is viewed as a form of "adaptive inactivity," then this paradox vanishes. A small sleep rebound may be necessary to compensate for processes that can only occur, or occur optimally, in sleep, but most sleep time is determined in each species by the evolved trade-offs between active waking and adaptive inactivity.

The variation in rebound within and across species needs to be more carefully studied. Some aspects of

rebound have been shown to be due to the deprivation procedure rather than the sleep loss. For example 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.[83,84] It is possible that in some species other aspects of rebound are driven by hormonal release linked to sleep rather than by some intrinsic property of sleep.

CONCLUSION

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 and minimal predator risk. 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, dealing with predators, and responding to environmental changes. A major function of REM sleep may be to allow this rapid response by periodic brainstem activation. Many organisms can reduce sleep for long periods of time without rebound during periods of migration or other periods in which a selective advantage can be obtained by continuous waking.

The big brown bat 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.[21] Not surprisingly, this waking is synchronized to the period when flies are active. It is not likely that this short waking period, one of the shortest yet observed, can be 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 physiological maintenance requirement. An approach that takes the environmental conditions in which each species evolved into account can better explain the variance in sleep time between mammals.

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 is highly probable that some functions have migrated into or out of sleep in various animals. Recent work has suggested that neurogenesis,[85] synaptic downscaling,[86] immune system activation[87] and reversal of oxidative stress[88,89] may be accomplished in sleep in mammals. It remains to be seen if these or any other vital functions can only be performed 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 may better explain this variation.

Further relevant literature can be found at http://www.semel.ucla.edu/sleepresearch.

> ❖ **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.

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