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Sleep Phylogenic Evolution and Ontogeny

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The central scientific issue in sleep research is "Why do we sleep?" We all know we sleep to keep from being sleepy; however, this is like saying we eat to keep from being hungry. In the case of eating, we have an understanding of the need for food, including energy acquisition and the ingestion of vital nutrients. But we do not have a comparable understanding of why we sleep.

The seemingly straightforward way to investigate sleep function is by deprivation. However, deprivation necessarily involves stress. We know that awakening is accompanied by cortisol release[1–4] and phasic activation of a large number of neuronal groups.[5,6] Human studies rarely control for the stress of maintaining awakening and alertness. The controls used in animal deprivation studies frequently involve stimulating a control animal in the same pattern as the animal being deprived, but confining this stimulation to periods of spontaneous waking. But an animal that is awake will not show the autonomic or hormonal response to the awakening stimulus seen in the sleeping experimental animal. Long-term deprivation of rats can require more than 1000 awakenings a day.[7] So this leaves the investigator studying the effect of repeated awakening plus sleep loss, not just the effect of sleep loss.

Another approach is to correlate spontaneous sleep duration with a variety of physiological variables. Do people who sleep a lot learn faster than people who sleep less? Are they healthier? Recent studies contradict both of these assertions.[8,9] Other human studies have demonstrated that there is considerable interindividual variation in the response to sleep deprivation. Some individuals are able to be relatively vigilant and functional when their sleep is reduced, whereas others are not. These groups do not greatly differ in baseline sleep amounts.[10]

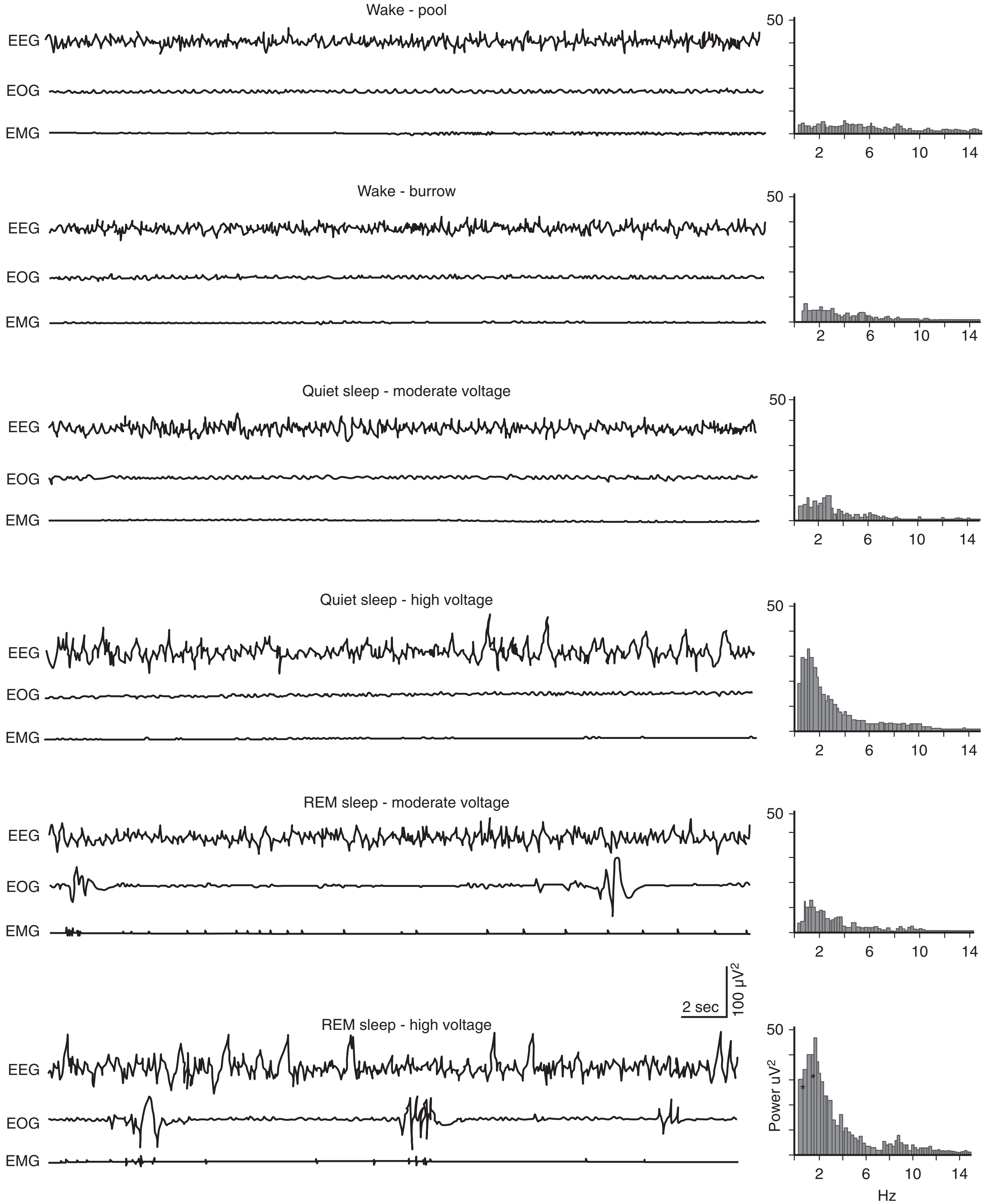
Rapid Eye Movement Sleep

One key unknown in sleep function is the role of rapid eye movement (REM) sleep. Why do animals vary in the amount of REM sleep they have? The discovery of REM sleep and its link to dreaming in 1953[11] led to considerable speculation that this was a uniquely human aspect of sleep and was presumably related to higher cognitive functions, even to schizophrenia and other mental disorders. But further phylogenetic work revealed that REM sleep was present in the most "primitive" mammals, including the platypus and echidna, and in these species it was quite intense, with rapid eye movements and neuronal activation comparable with that seen in cats, rats, and humans.[12,13]

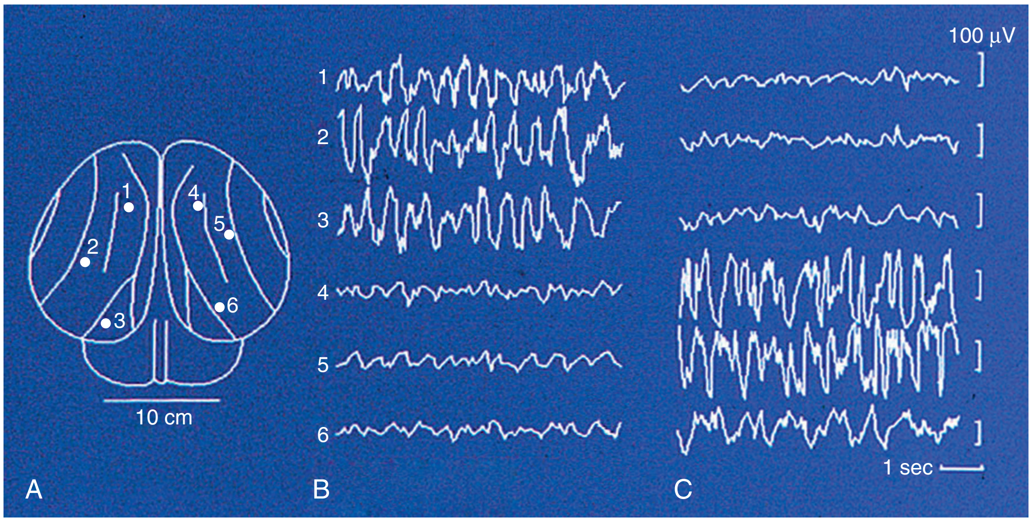
The platypus has more than 7 hours/day of REM sleep, compared with the approximately hour and a half in humans (Fig. 2.1). Recent work has shown that the ostrich, considered a relatively primitive (plesiomorphic) bird, also has large amounts of REM sleep and "sleeps like the platypus."[14]

Marine Mammals

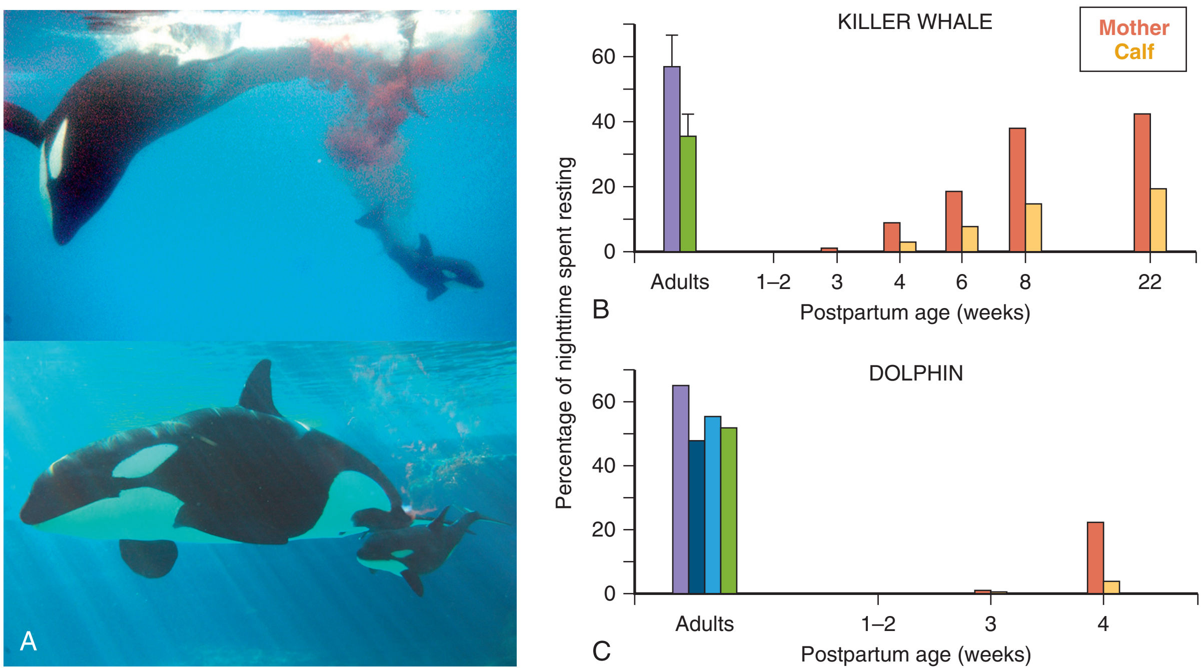
- Although most land mammals have a REM sleep-like state, this had not been seen in certain marine mammals. Early work in dolphins indicated that these animals had a very unusual electroencephalogram (EEG) pattern. They show slow waves, similar to those seen in deep (stage N3) human sleep. But these waves appear in only one hemisphere at a time, never bilaterally.[15] This pattern has been labeled unihemispheric slow waves or unihemispheric slow wave sleep (USWS).
- In contrast, all land mammals show bilateral high voltage EEG during sleep. Although this has been termed "unihemispheric sleep," it could be argued that these animals do not meet the conventional behavioral definition of sleep. They remain responsive during this EEG pattern and are able to time their breaths to avoid aspiration of water as waves break around them, a task not required in land mammals. Their posture is



• **Figure 2.1** The platypus has the largest amount of REM sleep yet reported. This graph shows power spectra of EEG in each trace. *EEG,* Electroencephalogram; *EMG,* electromyogram; *EOG,* electrooculogram; *REM,* rapid eye movement. (Copyright Jerome M. Siegel.)



• **Figure 2.2** Unihemispheric Slow Waves in the Dolphin. The dolphin never shows the bilateral high voltage slow waves that characterize slow wave sleep in mammals. Their electroencephalogram state is not consistently correlated with the behavioral quiescence of sleep.[16,45] **A,** Indicates location of recording electrodes. **B** and **C,** Indicate left and right hemisphere sleep. (Modified from Mukhametov LM, Supin AY, Polyakova IG. Interhemispheric asymmetry of the electroencephalographic sleep patterns in dolphins. *Brain Res.* 1977;134:581–584.)



• **Figure 2.3** **A,** Birth of the killer whale Kasatka in a puff of blood. We were able to monitor Kasatka and Nakai's activity for more than 7 weeks postpartum, finding continuous activity throughout that period. **B,** Postpartum activity of Nakai *(yellow)* and his mother Kasatka *(red)* in comparison to control adult killer whales *(blue and green)* housed at the same facility. Resting time is absent for months after birth in both mother and calf, with no rebound after this period. **C,** A similar pattern is seen in dolphins. (**A,** Photo courtesy of SeaWorld, San Diego.)

symmetrical, and the presence of USWS cannot be easily identified by observation of the animal's posture or activty (Fig. 2.2).[16,17]

- A further peculiarity of sleep in cetaceans (whales and dolphins) is that there had been no reports of REM sleep in this clade. We know that sleep duration and the percentage of sleep time devoted to REM sleep are maximal at birth.[18] So if REM sleep is present in cetaceans, it should be readily detectable at birth. Therefore we undertook studies of newborn killer whales and dolphins in an attempt to identify REM sleep (Fig. 2.3).
- We were very surprised to find no evidence for REM sleep in the newborn killer whale. Even more surprising was that there

was no evidence for sleep of any kind in the calf for at least 3 weeks. The mother also stopped sleeping during this period. Mother and calf remained in constant motion, coordinating their movement to stay in formation, avoiding obstacles and breathing normally. We saw the same pattern in dolphins.[19] A further surprise was that although periods of inactivity returned to baseline levels by about 5 months of age, there was no "rebound" of inactivity beyond baseline levels in either mother or calf. The ecological literature indicates that this period of continuous activity coincides with migrations in the wild. This migration period is particularly dangerous for newborn cetaceans. Killer whale calves can be killed by sharks and by other killer whales. So the continuous 24 hours/day alertness the mother and calf exhibit has obvious adaptive value not required in most land mammals.

- Further work showed that this ability to be active and responsive for many days was not confined to the postpartum period. It was shown that adult male and female dolphins can perform an auditory or visual discrimination task (the latter presented to either eye) for 24 hours a day for as long as 15 days, with no decrement in responsiveness during the period and no rebound of inactivity after the task was removed. Cetaceans do not sleep as this term is understood in humans.
- Periods of extended waking are not unique to cetaceans (whales and dolphins). Although the walrus and fur seal exhibit both non-REM and REM sleep (Fig. 2.4), they frequently stop sleeping, spontaneously, for more than 3 days,[20] unlike land mammals. Such behavioral patterns may be common in marine mammals because their environmental opportunities and risks are more linked to the tides than the day-night cycle. Fish may show a similar flexibility in sleep duration and timing.[21]
- Another marine mammal that we have studied is the fur seal. The fur seal may well deserve the distinction of having the most unusual and perhaps most informative sleep pattern seen in mammals. When the fur seal, which is related to the dog and other carnivores, sleeps on land, it has both REM and non-REM sleep, as seen in other carnivores. However, when it is in water, where it spends most of its life, it switches to unihemispheric EEG patterns resembling those of dolphins.
- REM sleep amounts are greatly reduced. In contrast to dolphins, this unihemispheric sleep pattern is accompanied by quiescence of the limbs controlled by the "sleeping" hemisphere. Therefore, whereas the label "unihemispheric sleep" is questionable in dolphins, which show no motor or postural asymmetry during their EEG asymmetry, the designation "unihemispheric sleep" fits the pattern seen in the fur seal.[22–24]
- The absence of REM sleep in the dolphin and its near elimination in water in the fur seal suggests that REM sleep serves a function not required when alertness and responsiveness is not reduced bilaterally.
- Bilateral sleep is associated with sleep inertia upon awakening.[25] The arousal linked to REM sleep,[26,27] its prevalence near the time of awakening,[26,28] and its relative absence following unihemispheric slow waves is consistent, with a role for REM sleep in reversal of sleep inertia.

• **Figure 2.4** Walrus. The walrus (*Odobenus rosmarus divergens*) shows spontaneous periods of waking lasting more than 3 days. (Copyright Jerome M. Siegel.)

The Neurochemistry of Electroencephalogram Control

We took advantage of the interhemispheric EEG pattern seen in fur seals to investigate the neurochemical substrates of this pattern. In land mammals we know that the release of a number of waking neurotransmitters is reduced in sleep.

However, we do not know if these changes in release are related to the changes in the cortical EEG, or whether they are simply secondary to the reduction in movement or sensory experience or of motivational drive in waking. Are the transmitters linked to waking asymmetrically release in unihemispheric sleep? To our surprise, we found that norepinephrine, serotonin, and histamine were symmetrically released in asymmetric sleep.[29,30] But acetylcholine release was greatly asymmetric, being maximal in the waking hemisphere.[31] In contrast, the release of all of these transmitters was comparably increased from quiet waking to active waking. This work identifies a unique role for acetylcholine in EEG activation.

Birds

Birds show great seasonal changes in sleep duration. The white crowned sparrow greatly reduces REM and non-REM sleep time during migrating season, acting in a "manic" manner, even when prevented from migrating. During this period, they do not show impairment in learning ability. After this period, they do not exhibit a rebound of lost sleep, similar to the lack of rebound in dolphins and killer whales after the postpartum period of sleep suppression.[32] Yet another example of this phenomenon has been observed in male polygynous pectoral sandpipers (Fig. 2.5). These birds have a virtually complete suppression of sleep during the annual mating period, with the birds that sleep the least producing the most offspring. During the 3-week period of sleep suppression they fought off rivals and showed little or no sleep, and no decrease in the effectiveness of their behavior.[32] Birds show no relationship between sleep duration and any of the parameters considered in mammals.[33]

Land Mammals

There is seasonal heterogeneity in the daily activity pattern of land mammals, particularly those living in regions with great seasonal changes in food availability. The arctic reindeer *Rangifer tarandus* spends 43% more time active in the summer than in the winter, likely accompanied by a great decrease in sleep and drowsy states relative to winter (Fig. 2.6).[34] Other mammals such as the ground squirrel and bear hibernate, entering the hibernation state through sleep.[35–37]

Phylogenetic Correlates of Sleep Duration

- When one compares the sleep of animals with their other attributes, it is clear that sleep duration is not correlated with brain size or brain–body weight ratio (Fig. 2.7).
- Closely related species can have widely divergent sleep durations. Statistical manipulations calculating REM sleep as total time versus percent of sleep time do not clarify the issue. Some striking examples of this can be seen in Figs. 2.8 and 2.9.[38,39] The guinea pig has precisely the same amount of REM sleep as the baboon. The eastern American mole has the same sleep durations as those reported in humans. The golden mantled ground squirrel has more than twice the sleep duration of the degu, a rodent of similar size. The house cat has approximately double the sleep duration of the genet, a related feline carnivore. Brain size is not correlated with total sleep or REM sleep duration (Fig. 2.10).
- These many examples are drawn from the set of 70 or so mammals whose sleep has been systematically studied (i.e. they are not rare exceptions to rules derived from some larger set).
- One analysis showed that big animals sleep less.[40] This is a relatively weak correlation, but implies a relation between sleep and mass specific metabolic rate, since metabolic rate is linked to mass. However, closer analysis reveals that the body mass–sleep duration relationship is only present in herbivores.[17,41]
- Big animals like the tiger and giant armadillo sleep a lot, undermining the likelihood that metabolic rate determines sleep time. This same analysis also showed that carnivores sleep more than omnivores, who sleep more than herbivores (Fig. 2.11).
- These data suggest that the ecological niche and particularly the caloric density of the customary food is a major determinant of sleep duration. If an animal eats grass and leaves, they have to spend a lot of time collecting, ingesting, and chewing their food. In contrast if a carnivore kills its prey, it need not spend time hunting again for as long as several days, and it is most adaptive for it to sleep and stay with its offspring as it digests and metabolizes its kill. The big brown bat (Fig. 2.12) is the current sleep champion, sleeping 20 hours a day, awake only at dusk and in the early evening when its insect prey are airborne.
- Another reasonable conjecture is that lifespan might be related to sleep duration across species. However, this is not the case.[40] A common misconception is that there is a linear relation between sleep duration and lifespan in humans. In fact, the relation forms a U-shaped curve, with a self-report of 7 hours optimal for survival, and both higher and lower amounts of sleep being correlated with reduced lifespan. A surprising but consistent finding of these very large epidemiological studies is that sleeping more than 7 hours is correlated with a shorter

• **Figure 2.5** The polygynous pectoral sandpiper shows 3-week-long periods of no sleep and high mating performance levels during the arctic summer. (Copyright Jerome M. Siegel.)

• **Figure 2.6** Reindeer (*Rangifer tarandus*) show 43% more activity in the summer, when food is available, than in the winter. (Copyright Jerome M. Siegel.)

• **Figure 2.7** Closely related animals do not have similar sleep patterns. *REM,* Rapid eye movement.[38,50] (Copyright Jerome M. Siegel.)

Rodentia

	High sleep: Golden mantled ground squirrel *Spermophilus lateralis*	Low sleep: Degu *Octodon degu*
Total sleep	15.9	7.7
REM sleep	3.0	0.9
Body weight	0.193	0.240
Brain weight	0.003	0.0025
Brain/body weight ratio	0.016	0.010
Lifespan	7	11
Caloric density of food	++	+

Carnivora

	High sleep: Cat *Felis catus*	Low sleep: Genet *Genetta genetta*
Total sleep	12.5	6.3
REM sleep	3.2	1.3
Body weight	3.3	1.3
Brain weight	0.030	0.016
Brain/body weight ratio	0.009	0.012
Lifespan	13	13
Caloric density of food	+++	++

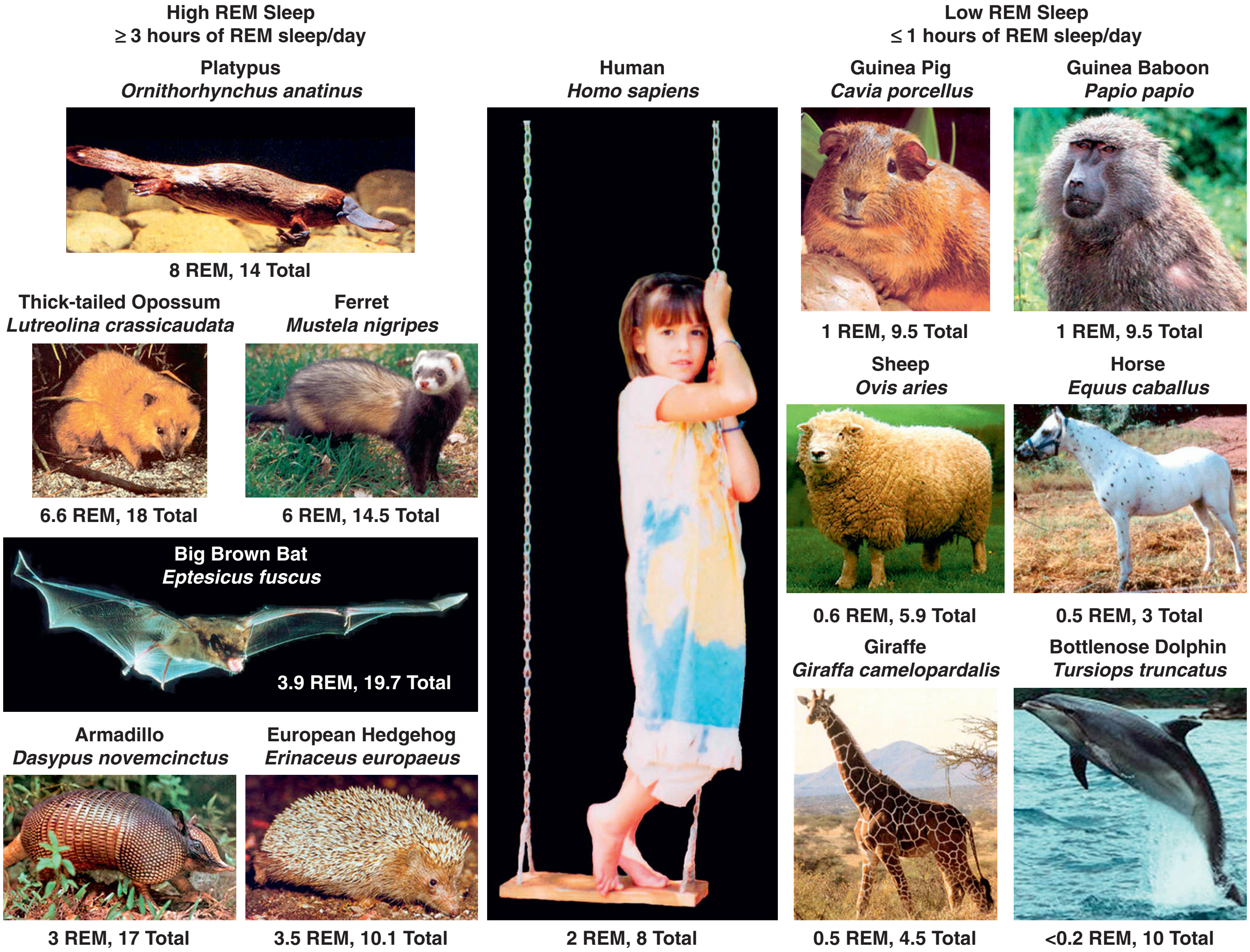
Chiroptera

	High sleep: Big brown bat *Eptesicus fuscus*	Low sleep: Greater short-nosed fruit bat *Cynopterus sphinx*
Total sleep	20	15.0
REM sleep	3.9	1.15
Body weight	0.0136	0.0424
Brain weight	0.238 mg	1.061 mg
Brain/body weight ratio	0.0175	0.025
Lifespan	20	10
Caloric density of food	+++	+

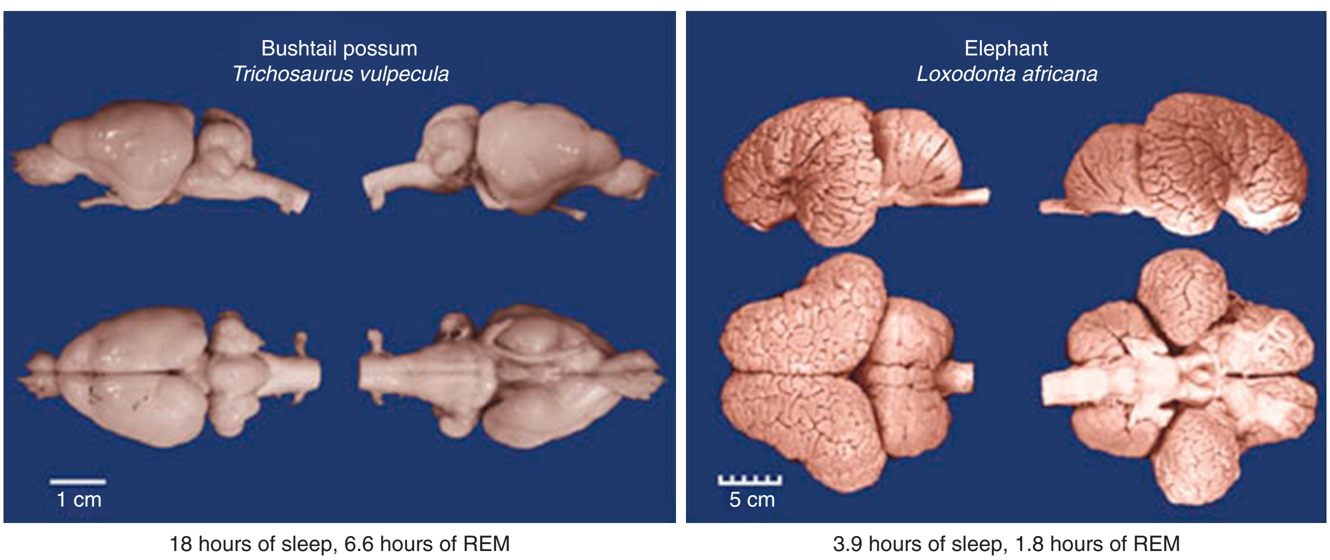
Aves

	High sleep: Burrowing owl *Athene cunicularia*	Low sleep: Greylag goose *Anser anser*
Total sleep	14.3	6.4
REM sleep	0.7	0.7
Body weight	0.120	3.3
Brain weight	0.003	0.011
Brain/body weight ratio	0.025	0.003
Lifespan	8	8
Caloric density of food	+++	+

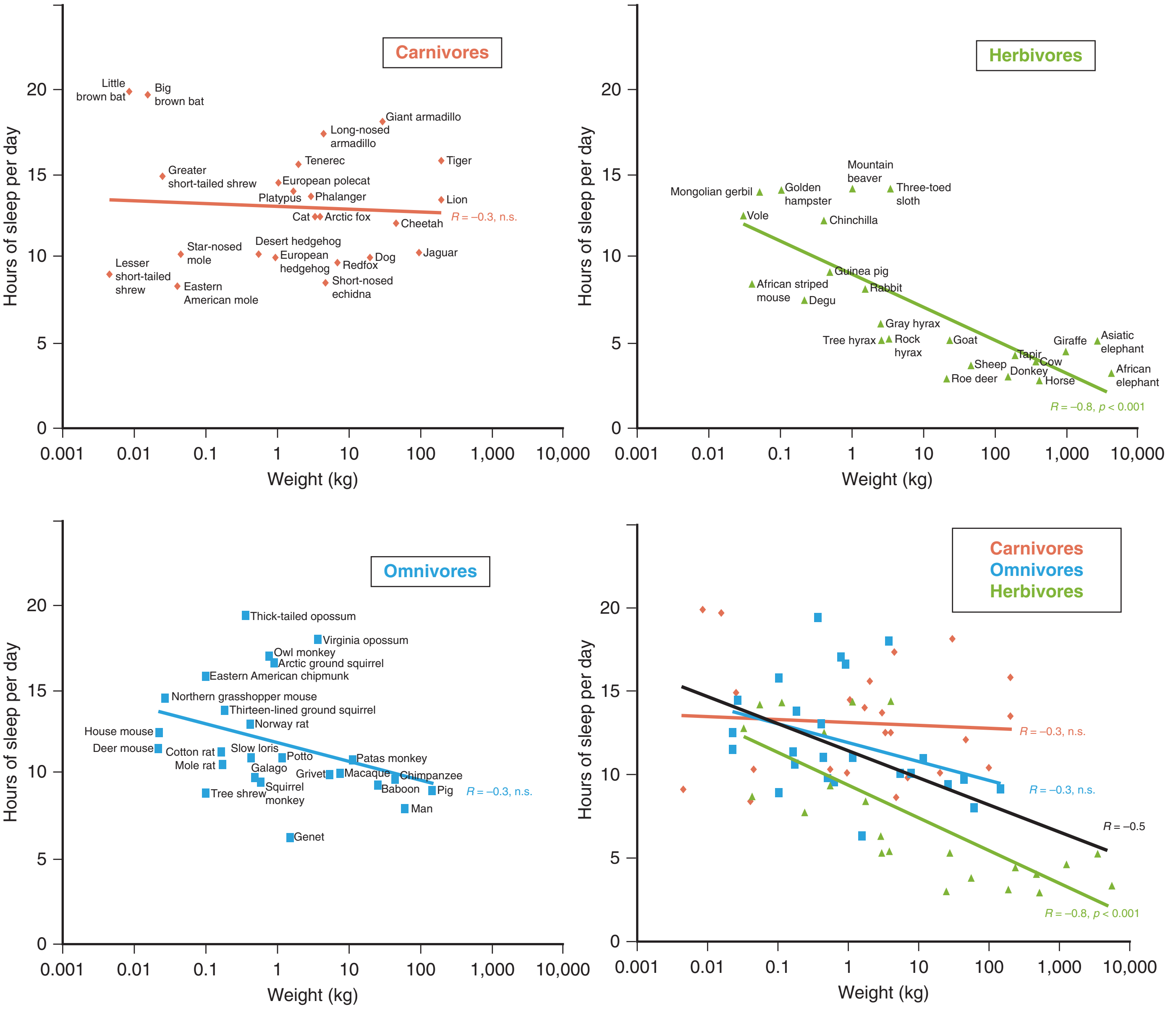
• **Figure 2.8** Physiological variables are not strongly correlated with sleep duration, even in related species. *REM,* Rapid eye movement.[50] (Copyright Jerome M. Siegel.)



• **Figure 2.9** Human REM and non-REM sleep amounts are not unique, despite our unusual attributes. *REM,* Rapid eye movement.[51] (Copyright Jerome M. Siegel.)



• **Figure 2.10** Brain size is not correlated with total sleep or REM sleep duration. *REM,* Rapid eye movement.[51] (Copyright Jerome M. Siegel.)



• **Figure 2.11** Carnivores sleep more than herbivores. Sleep duration is correlated with body size only in herbivores. The correlation is negative.[17] (Copyright Jerome M. Siegel.)

lifespan than sleeping less than 7 hours. This finding is robust, even after exclusion of subjects inclined toward sleep apnea or other pathologies.[42–44]

Clinical Significance

- These findings are of clinical significance, since the argument that the more you sleep the longer you will live is used to sell sleeping pills, including hypnotics acting on the benzodiazepine receptor.
- Although chronic use of sleeping pills only produces a small elevation of sleep duration, at least 15 studies have shown that chronic use substantially shortens the lifespan, whereas untreated insomnia does not.[42] There is, to my knowledge, no study showing increased lifespan with chronic use of sleeping pills (see https://www.semel.ucla.edu/sleepresearch/publication/newspaper-article/2010/huffington-post-are-sleeping-pills-good-you).
- One of the main factors driving sleeping pill use is the idea that sleeping times have greatly decreased in "modern" societies because of the use of artificial light, television, and most recently the Internet. However, the evidence for this is scant. Tools for accurately quantifying sleep time were developed long after the invention of electric lights. Although we cannot go back in time, several groups of hunter-gatherers still exist. These groups lack electricity and battery-powered devices. Some of them live in the very regions in which *Homo sapiens* evolved. If the supposition that modern life has greatly reduced sleep time is correct, these individuals should go to sleep at sunset and sleep 9, 10, or 11 hours. This is not what we found (Fig. 2.13).[45]

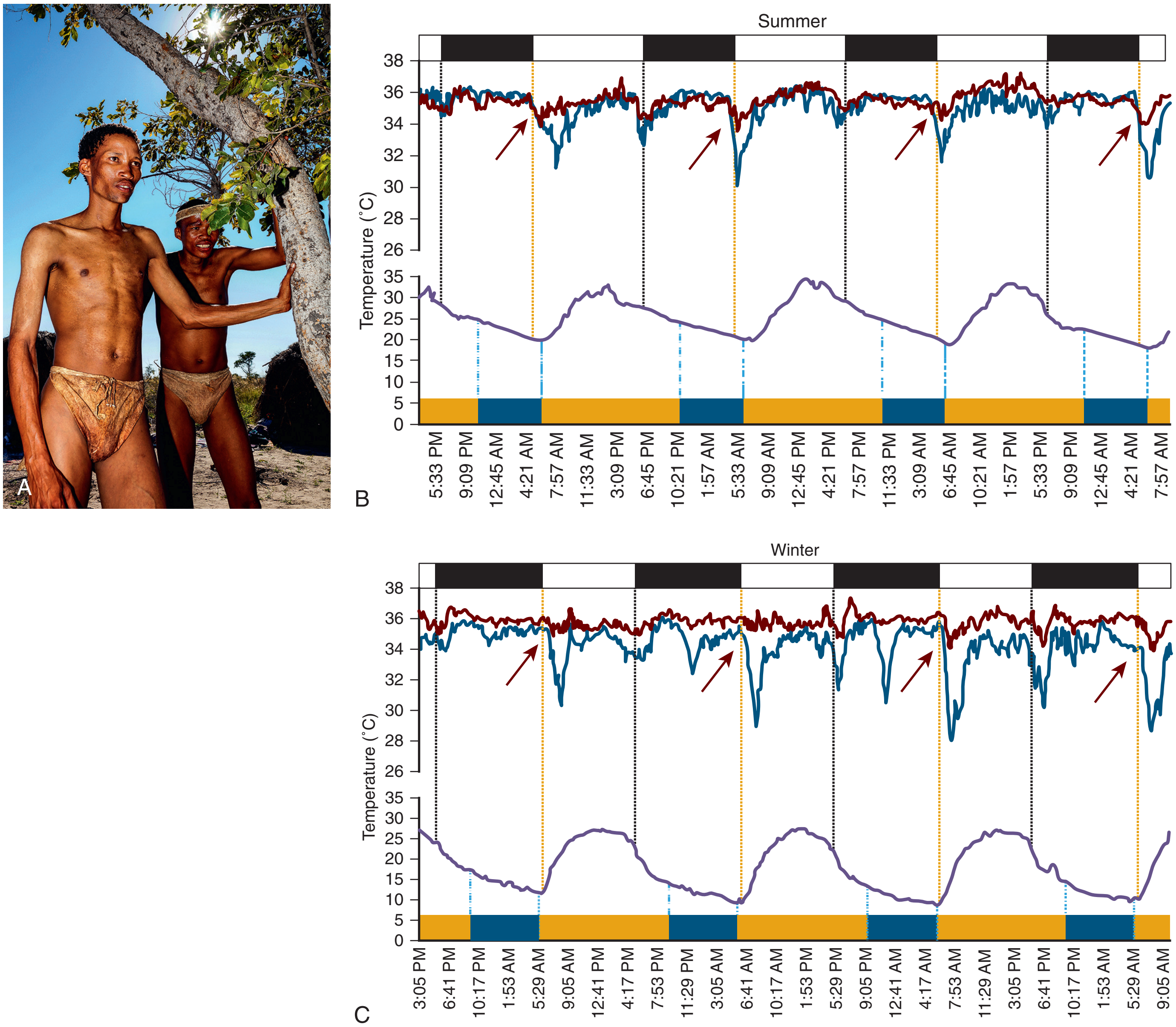
• **Figure 2.12** The big brown bat has the highest amount of sleep yet documented, at 20 hours/day.[52] (Copyright Jerome M. Siegel.)

Sleep in Preindustrial People

- None of the individuals in the three groups studied habitually go to sleep at sunset. Rather, sleep onset occurred, on average, 3.3 hours after sunset. The average sleep period duration was 7.7 hours, an amount at the low end of those reported using identical actigraph measurements and scoring algorithms. Winter sleep durations are an hour longer than summer durations.
- Most important, in all seasons, sleep onset occurs during a period of falling environmental temperature. Sleep continues, without long interruptions, until temperature hits the daily nadir, when awakening occurs. Sleeping during the coldest part of the day is consistent with an energy conservation role. To use a phrase popularized by Desmond Morris, the "naked ape" would be at a great disadvantage if it was active during the coldest part of the day. Metabolically costly heat loss is minimized by allowing body temperature and brain energy consumption to fall, as occurs in sleep.
- The daily rhythm of temperature experienced by hunter-gatherers, and also by the primate ancestors of all humans, has largely been abolished in "modern" civilizations. Given the extent to which this rhythm is so tightly linked to temperature (rather than light), it may be hypothesized that the removal of this rhythm in "modern" society may contribute to sleep pathology.
- Although sleep disorder centers routinely recommend a reduction in the thermostat setting at night, the magnitude and time course of this reduction may not resemble the time course of temperature that our ancestors may have experienced. It is also important to appreciate that this temperature variation is experienced by hunter-gatherers from birth, and may induce physiological changes that cannot be simply transferred by exposing adults to such changes. Further work is necessary to fully understand and therapeutically exploit the dynamics of this relationship.
- We see no data to support the assumption that human sleep has been greatly reduced by the amenities of modern life. A more recent study of sleep over the last 50 years has also found no change, consistent with our study and conflicting with the notion that recent technological developments have reduced sleep.[46]
- Habitual napping and insomnia are nearly nonexistent in all three of the groups examined. It is well known that daily napping is a common cause of insomnia.[47,48] Napping is correlated with shorter lifespan.[49]

Conclusions

- Sleep and sleep-like states vary greatly across the animal kingdom.
- Most mammals and birds have not been systematically studied. But both REM and non-REM sleep have been seen in most land mammals that have been polygraphically investigated.
- Marine mammals provide important insights into the nature of sleep. Cetaceans (dolphins and whales) are able to maintain a vigilant state, even while having unihemispheric slow waves. Dolphins do not appear to have REM sleep and can remain vigilant and responsive for more than 15 days with no evidence of rebound sleep.
- Sleep depth and duration vary across species and seasons.
- Sleep duration across species is not correlated with brain size or brain–body weight ratio.
- The strongest correlate of sleep duration across species is diet, suggesting that herbivores have evolved to sleep very little so they can spend large amounts of time eating and chewing.



• **Figure 2.13** **A,** Hunter-gatherers of Namibia. **B** and **C,** Sleep in hunter-gatherers of Namibia. *Black* and *white* bars indicate the period of night and day. *Blue* and *orange* bars indicate periods of sleep and waking. *Violet* color indicates environmental temperature. Note that sleep occurs during a period of falling temperature and terminates when temperature hits the daily minimum. Sleep onset occurs 3.3 hours after sunset, on average. Sleep durations are near the low end of what has been reported in "modern" societies. Vasoconstriction, indicated by cooling of the fingers, occurs at wake onset in both summer and winter.[45] (**A,** Photo courtesy of Josh Davimes.)

- Preindustrial humans sleep nearly 1 hour more in the winter than in the summer. Their average amount of sleep does not exceed average sleep amounts reported in industrial societies.
- Insomnia and napping are rare in preindustrial groups.
- Awakening during the night is also rare in these groups, with wake after sleep onset not differing from that of "modern" populations.
- The daily temperature rhythm is a potent regulator of sleep in preindustrial societies, suggesting that the loss of this rhythm by artificial temperature regulation in modern societies may be a factor in sleep disorders.

Suggested Reading

Lesku JA, Meyer LC, Fuller A, et al. Ostriches sleep like platypuses. *PLoS ONE*. 2011;6:e23203.

Lyamin O, Pryaslova J, Lance V, Siegel J. Animal behaviour: continuous activity in cetaceans after birth. *Nature*. 2005;435:1177.

Siegel JM. Clues to the functions of mammalian sleep. *Nature*. 2005;437:1264-1271.

Siegel JM. Sleep viewed as a state of adaptive inactivity. *Nat Rev Neurosci*. 2009;10:747-753.

Yetish G, Kaplan H, Gurven M, et al. Natural sleep and its seasonal variations in three pre-industrial societies. *Curr Biol*. 2015;25:2862-2868.