Chapter

7

Evolutionary perspectives on the function of REM sleep

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Summary

In most mammals, sleep is composed of two distinct states, rapid eye movement (REM) sleep and slow-wave sleep (SWS). The differentiated nature of mammalian sleep suggests that each state performs a different function, or perhaps different, but complementary components of a unified function. Despite extensive research, the function(s) provided by sleep and its respective sub-states remains the subject of debate (Cirelli and Tononi, 2008; Mignot, 2008; Siegel, 2009; Stickgold and Walker, 2007). One approach to unraveling the function of each sleep state is to trace its evolution. Through identifying the type(s) of animals in which each state evolved, we may reveal biological traits that coevolved with a particular sleep state. Cases of convergent evolution may be particularly informative because they provide the opportunity to isolate traits shared by only those animals that evolved a particular sleep state. The independent coevolution of certain sleep states and traits may be functionally linked. Conversely, the subsequent coevolutionary loss of a particular sleep state and certain traits may also reveal traits that benefit from a particular sleep state. Moreover, assuming that sleep serves an important function, determining how such animals compensate for the loss of a particular sleep state may yield clues to its purpose. Finally, another approach is to identify biological traits that account for the variation in time spent in, and presumably need for, each state. Traits that influence the allocation of time to a particular state may suggest a function for that state. The following chapter summarizes insights into the function of REM sleep gleaned from these comparative approaches.

Phenomenology and evolutionary history of REM sleep

Therian mammals (marsupials and eutherians)

The class Mammalia is composed of three extant groups, monotremes, marsupials, and eutherians (placentals). The electrophysiological and physiological traits that occur during REM sleep, as we know it in therian (marsupial and eutherian) mammals, are typically used as criteria for determining whether other animals exhibit a similar state. Traditional measures of sleep, such as the electroencephalogram (EEG), electromyogram (EMG), and electrooculogram (EOG), have been studied in a diverse range of mammalian species, whereas traits that require more invasive methods, such as deep brain recordings, have only been examined in a few species (Siegel, 2011). In therian mammals, perhaps the defining feature of REM sleep is cortical activation (low-amplitude, high-frequency EEG activity similar to that occurring during wakefulness) occurring in an animal with elevated arousal thresholds (i.e., the paradox that gave REM sleep its other name, paradoxical sleep). In addition to cortical activation, skeletomuscle tone is greatly reduced or absent throughout most REM sleep, although such periods of tonic REM sleep are briefly interrupted by periods of phasic REM sleep characterized by rapid eye movements, twitching of the limbs and whiskers, chewing motions, and irregularities in respiratory and heart rates. In eutherian mammals, rapid eye movements occur in response to spikes of neuronal activity that propagate from the pons through the lateral

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geniculate nucleus of the thalamus to the occipital cortex (i.e., ponto-geniculo-occipital (PGO) spikes). The phasic events occurring during REM sleep are also associated with bursts of fast, irregular neuronal activity in the brain stem. In addition to these electrophysiological events, a hippocampal theta rhythm, similar to that occurring during ambulation while awake, also occurs during REM sleep. REM sleep is associated with penile erections in most eutherian mammals, but not armadillos (*Chaetophractus villosus*), where erections occur during SWS, a difference that apparently reflects alternative erectile mechanisms (vascular vs. muscular in eutherians and armadillos, respectively), rather than differences in REM sleep, per se (Affanni *et al.*, 2001). During REM sleep, brain temperature increases and thermoregulation is suppressed or depressed (Parmeggiani, 2003). The duration of REM sleep episodes and total amount of REM sleep increases across the major sleep period. The time spent in REM sleep increases following sleep deprivation, indicating that as with SWS, REM sleep is homeostatically regulated (Tobler, 2011). Although some studies have found large amounts of REM sleep in South American marsupials, preliminary data from Australasian marsupials suggest that REM sleep is not prevalent in all marsupials (Lesku *et al.*, 2006). Consequently, it is unclear whether the common ancestor to therian mammals engaged in disproportionately large amounts of REM sleep.

Monotremes

The presence of REM sleep with cortical activation in most therian mammals studied (see section on Evolutionary loss of REM sleep, below), suggested that it evolved before the appearance of marsupial and eutherian mammals. To further clarify the origin of REM sleep, Allison *et al.* (1972) examined sleep in the short-beaked echidna (*Tachyglossus aculeatus*), one of the few remaining species of monotremes. Monotremes are the extant representatives of Prototheria, a group of egg-laying mammals that diverged early from the mammalian lineage, before the therian lineage diverged into marsupial and eutherian mammals. If REM sleep, as we know it in therian mammals, was present in the ancestor to all mammals, then monotremes should show a similar state. Interestingly, while Allison *et al.* identified clear EEG signs of SWS, no unequivocal signs of REM sleep could be found despite using a combination of epidurally seated EEG electrodes over the frontal, parietal, and occipital cortex; depth electrodes in the pyriform cortex and dorsal hippocampus; and EOG, EMG, and EKG, as well as brain temperature measured from the frontal cortex. Allison *et al.* carefully examined a state that bore some gross resemblance to REM sleep (i.e., quiescent periods with EEG activation), but concluded that it reflected quiet wakefulness instead; skeletomuscular twitches, eye movements, hippocampal theta rhythm, increased arousal thresholds, elevated brain temperature, and variability in cardiorespiratory rates were not present during the REM sleep-like state, as would be expected if the state reflected therian mammal-like REM sleep. Moreover, selective deprivation of this state in one echidna for 48 hours failed to induce a compensatory increase in this state during recovery, as expected if it reflected a homeostatically regulated state comparable to REM sleep in eutherian mammals. Collectively, these results indicated that the REM sleep-like state was more akin to quiet wakefulness than to REM sleep. Albeit limited to a single species, the absence of REM sleep in the echidna tentatively suggested that REM sleep evolved only after the appearance of the therian lineage.

A subsequent investigation into the evolution of REM sleep reexamined EEG-defined sleep in the echidna (Siegel *et al.*, 1996). Importantly, however, in addition to epidurally seated cortical electrodes, Siegel *et al.* recorded neuronal unit activity from the pontine tegmentum – an area involved in the initiation of REM sleep in eutherian mammals – and the midbrain reticular formation. Consistent with the findings of Allison *et al.* (1972), Siegel *et al.* found only EEG signs of SWS in sleeping echidnas. However, concurrent with cortical SWS, brain-stem neurons fired in an irregular REM sleep-like pattern with a rate intermediate between the slow, regular rate observed in SWS and the fast, irregular rate observed during REM sleep with cortical activation in cats and dogs (Figure 7.1*a, b*). Sleep data from another species of monotreme – the duck-billed platypus (*Ornithorhynchus anatinus*) – yielded consistent results. As in the echidna, the cortex of sleeping platypuses only showed EEG activity indicative of SWS (Siegel *et al.*, 1999). Cortical SWS was frequently accompanied by bursts of rapid eye movements and twitching of the bill and head, similar to the phasic skeletomuscular activity observed in therian mammals during REM sleep (see www.semel.ucla.edu/sleepresearch). Although brain-stem neuronal activity was not examined directly, this behavior suggests that the platypus brain stem was in an REM sleep-like state. Thus, as in the echidna, the platypus apparently

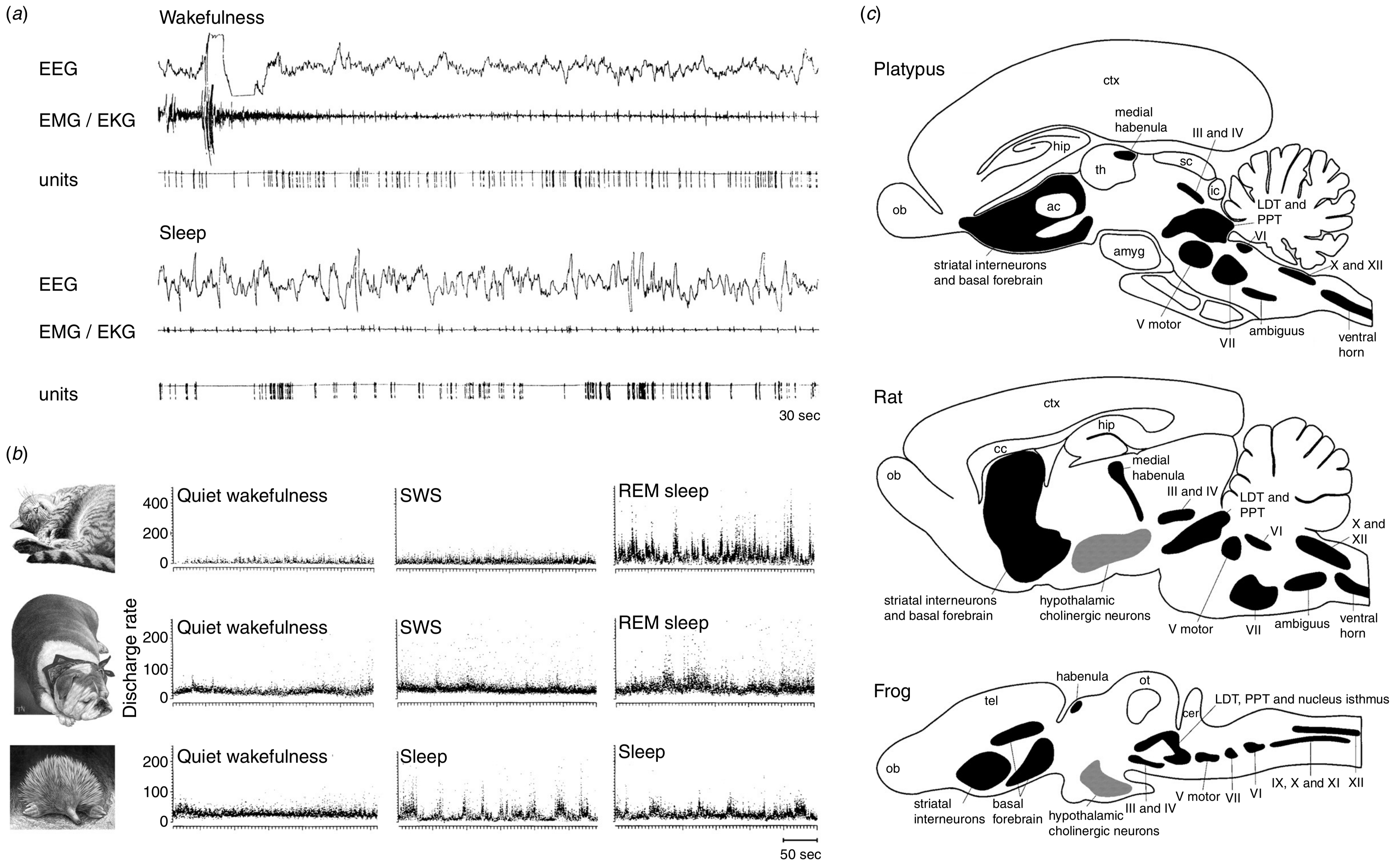

Figure 7.1 The electrophysiological and neuroanatomical correlates of sleep in monotremes. (*a*) Sleep in the echidna is associated with electroencephalogram (EEG) activity characteristic of slow-wave sleep (SWS) occurring concurrently with irregular brain-stem unit activity. (*b*) The rate of brain-stem unit activity observed in sleeping echidnas (bottom) is intermediate between the slow, regular rate observed during SWS and the fast, irregular rate observed during rapid eye movement (REM) sleep in dogs (middle) and cats (top). (*a*) and (*b*) From Siegel *et al.* (1996). (*c*) Cholinergic neuronal groups (shaded in black and gray) in the platypus, rat, and frog. The presence of cortical SWS occurring concurrently with REM sleep-like brain-stem activity in the echidna, and a similar state in the platypus, may reflect the absence of a cholinergic neuronal group in the hypothalamus of monotremes. The presence of this neuronal group in all other tetrapods examined (e.g., depicted in gray for the rat and frog), suggests that monotremes lost this trait, in which case the unique features of sleep in monotremes may reflect a derived trait, rather than the sleep state present in the common ancestor to all mammals. Abbreviations: ac (anterior commissure), amyg (amygdala), cc (corpus callosum), cer (cerebellum), ctx (cortex), EKG (electrocardiogram), EMG (electromyogram), hip (hippocampus), ic (inferior colliculus), LDT (lateral dorsal tegmental nucleus), ob (olfactory bulb), ot (optic tectum), PPT (pedunculopontine tegmentum), sc (superior colliculus), tel (telencephalon), th (thalamus). Cranial nerve nuclei are denoted with their respective Roman numerals. (*c*) From Manger *et al.* (2002). Images of the cat, dog, and echidna are courtesy of Grass-Telefactor, An Astro-Med, Inc. Product Group.

exhibits a heterogeneous sleep state with cortical correlates of SWS occurring concurrently with REM sleep-related brain-stem activity. Moreover, albeit limited by the small number of extant species, the available data suggests that temporally distinct SWS and REM sleep, as seen in therian mammals, evolved from a single, heterogeneous monotreme-like sleep state.

Interestingly, the platypus, or at least its brain stem, may spend a large amount of time in REM sleep. By defining REM sleep as a sleep period with at least one eye movement per minute occurring concurrently with cortical SWS-related EEG activity, Siegel *et al.* (1999) estimated that platypuses spend up to eight hours in REM sleep a day, more than any other animal studied. However, the utility of comparing the time spent in REM sleep based on cortical activation, as seen in therian mammals, to REM sleep estimates derived only from the temporal pattern of twitching in the platypus is unclear. Certainly, based on EEG activity, those same eight hours could be interpreted as SWS. Given that REM sleep-related phasic events are associated with irregular brain-stem activity in placental mammals, perhaps the most accurate way to describe these eight hours is to say that the brain stem (although not recorded directly in platypuses) was in REM sleep, while the cortex was in SWS. Finally, given the absence of direct measures of brain-stem activity, it is conceivable that some of the intervening time between phasic events reflected a SWS state both in the cortex and the brain stem. Indeed, precedent for aspects of REM sleep occurring in short bursts lasting less than ten seconds can be found in birds (see section on Avian reptiles, below). Nonetheless, the results from the echidna and platypus suggest that REM sleep is present, at least at the level of the brain stem, and may have been present in the ancestor to all mammals.

In contrast to the earlier studies (Allison *et al.*, 1972; Siegel *et al.*, 1996), a more recent study of sleep in the echidna reportedly identified REM sleep *with* cortical activation, as seen in therian mammals (Nicol *et al.*, 2000). Because such REM sleep only occurred at temperatures within the thermoneutral zone of echidnas, Nicol *et al.* (2000) argued that unnatural recording temperatures employed in the earlier studies prevented the expression of REM sleep. However, because eye state and arousal thresholds were not determined, it is unclear if the putative REM sleep state reported in Nicol *et al.* (2000) reflected REM sleep or an animal sitting quietly awake, as determined by Allison *et al.* (1972). Furthermore, the notion that REM sleep with cortical activation was missed in the earlier studies due to the echidnas being housed in temperatures outside their thermoneutral zone is challenged by the absence of REM sleep with cortical activation in platypuses housed in a naturalistic burrow system exposed to natural ambient temperatures (Siegel *et al.*, 1999). Finally, as next discussed, the results from Allison *et al.* and Siegel *et al.* are consistent with recently described neuroanatomical differences between monotreme and therian mammals.

The absence of cortical activation during REM sleep in monotremes suggests that this trait was first acquired in therian mammals. However, an alternative explanation that warrants consideration is the possibility that REM sleep-related cortical activation was present in the common ancestor to all mammals, but monotremes subsequently lost this trait. Although such a scenario may seem speculative, the adaptive loss of genes and associated functions has been a driving force in the evolution of vertebrates, including monotremes (Ordoñez *et al.*, 2008). With regard to sleep, neuroanatomical evidence suggests that monotremes lost a neuronal group involved in REM sleep-related cortical activation in therian mammals. Although the catecholaminergic and serotonergic systems are largely similar in monotreme and eutherian mammals, echidnas and platypuses lack a cholinergic cell group in the hypothalamus (Figure 7.1*c*; Manger *et al.*, 2002). The absence of this neuronal group may create a hiatus in cholinergic transmission between the brain stem and cortex, and thereby explain the unusual phenomenology of sleep in monotremes (Manger *et al.*, 2002). Indeed, a monotreme-like heterogeneous sleep state with REM sleep-like activity in the brain stem occurring concurrently with cortical SWS occurs in cats following lesions in this area (Jouvet, 1962; Siegel, 2011). Interestingly, the absence of this cholinergic group appears to reflect an evolutionary loss in the ancestors to monotremes, because it is present in all other vertebrates examined, including fish, amphibians, reptiles, birds, and eutherian mammals (Manger *et al.*, 2002). Note that this does not necessarily indicate that REM sleep, as we know it in therian mammals, is present in all vertebrate groups; indeed, evidence for REM sleep in fish, amphibians, and non-avian reptiles is equivocal or absent (see section on Fish, amphibians, and non-avian reptiles, below). Rather, the cholinergic hypothalamic group may be necessary, but not sufficient, for generating REM sleep with cortical activation. Fish, amphibians, and non-avian reptiles presumably lack other traits necessary for generating REM sleep. Regardless of whether monotremes lost or never acquired REM sleep-related cortical activation, its apparent absence poses a challenge for functional theories that posit a role for cortical activation in the function of REM sleep.

Fish, amphibians, and non-avian reptiles

Research on sleep in monotremes suggests that aspects of REM sleep evolved prior to the divergence of prototherian and therian mammals. The following section reviews our current understanding of the evolution of REM sleep (and SWS) in vertebrates through examining sleep in non-avian reptiles, amphibians, and fish. Historically, reptiles were thought to represent the ancestors to mammals. However, Reptilia and Mammalia are actually sister groups forming Amniota that descended from sauropsids and synapsids, respectively (Figure 7.3). Reptilia is composed of Archosauria (crocodilians and birds) and Lepidosauria (lizards and snakes, and tuataras). The relationship between turtles and the rest of Reptilia remains debated, with molecular data supporting their placement as the sister group to Archosauria, and morphological data placing them as either the sister group to Lepidosauria or the sister group to all other reptiles, as historically thought (Lyson and Gilbert, 2009).

The electrophysiological correlates of sleep have been investigated in all reptilian groups with the exception of tuataras. In contrast, few amphibians and fish have been studied (Hartse, 1994). Although REM sleep has been reported in some fish based on the occurrence of eye movements during sleep, it is unclear whether this behavior reflects REM sleep or an unrelated phenomenon. Similarly, while some studies report REM sleep in non-avian reptiles, based on the occurrence of eye and limb movements during sleep, it remains unclear whether such behaviors reflect REM sleep-related twitching similar to that observed in mammals or brief arousals from sleep. Moreover, other researchers failed to detect such behaviors in sleeping reptiles. Notably, Eiland *et al.* (2001) did not observe movements in sleeping turtles or neuronal activity in the brain stem comparable to that observed during sleep in the echidna or REM sleep in eutherian mammals. Perhaps the only electrophysiological feature of sleep in reptiles that bears some gross similarity to mammalian sleep is the intermittent, high-amplitude, sharp-wave often recorded in the EEG of sleeping reptiles (Hartse, 1994). Rather than reflecting REM sleep-related PGO waves, however, these sharp waves appear to be homologous with the hippocampal sharp waves observed during mammalian SWS (Hartse, 1994; Rattenborg, 2007). Consequently, given the available data, unequivocal evidence for REM sleep in non-avian reptiles is missing. Furthermore, the available evidence suggests that brain-stem correlates of REM sleep evolved in the mammalian lineage prior to the divergence of the prototherian and therian mammals.

Avian reptiles

Although historically considered their own taxonomic group, birds are actually a derived type of reptile that evolved from theropod dinosaurs (Sereno, 1999). Along with their closest living relatives, the crocodilians, birds are the only living members of Archosauria. Interestingly, although birds are clearly perched on a branch of the reptilian phylogenetic tree, avian sleep patterns are more similar to those of their distant therian mammal relatives, than they are to crocodilians or any other group of reptiles. The electrophysiological correlates of sleep have been examined in 12 avian orders including struthioniformes (i.e., ostriches; unpublished data), representatives of the earliest branch of living birds. Although birds lack a truly laminar structure comparable to the mammalian neocortex, the avian pallium – the developmental and functional homologue of the (pallial) neocortex (Jarvis *et al.*, 2005; Medina and Abellán, 2009) – generates EEG activity remarkably similar to that observed in mammals during both wakefulness and sleep (Rattenborg, 2006). As in therian mammals, all birds examined exhibit unequivocal SWS and REM sleep (Figure 7.2), suggesting that both states were present in the common ancestor to modern birds. When compared to wakefulness, the EEG during avian SWS is characterized by high-amplitude, low-frequency activity similar to that observed during mammalian SWS. This pattern is in marked contrast to the EEG pattern observed during sleep in reptiles, which is usually characterized by the absence of high-amplitude, low-frequency EEG activity, and the presence of intermittent, high-amplitude hippocampal sharp waves (Hartse, 1994; Rattenborg, 2007). In addition to the gross similarities in SWS-related EEG activity, recent studies demonstrated that, as in eutherian mammals (Tobler, 2011), SWS is homeostatically regulated in birds (Martinez-Gonzalez *et al.*, 2008), indicating that

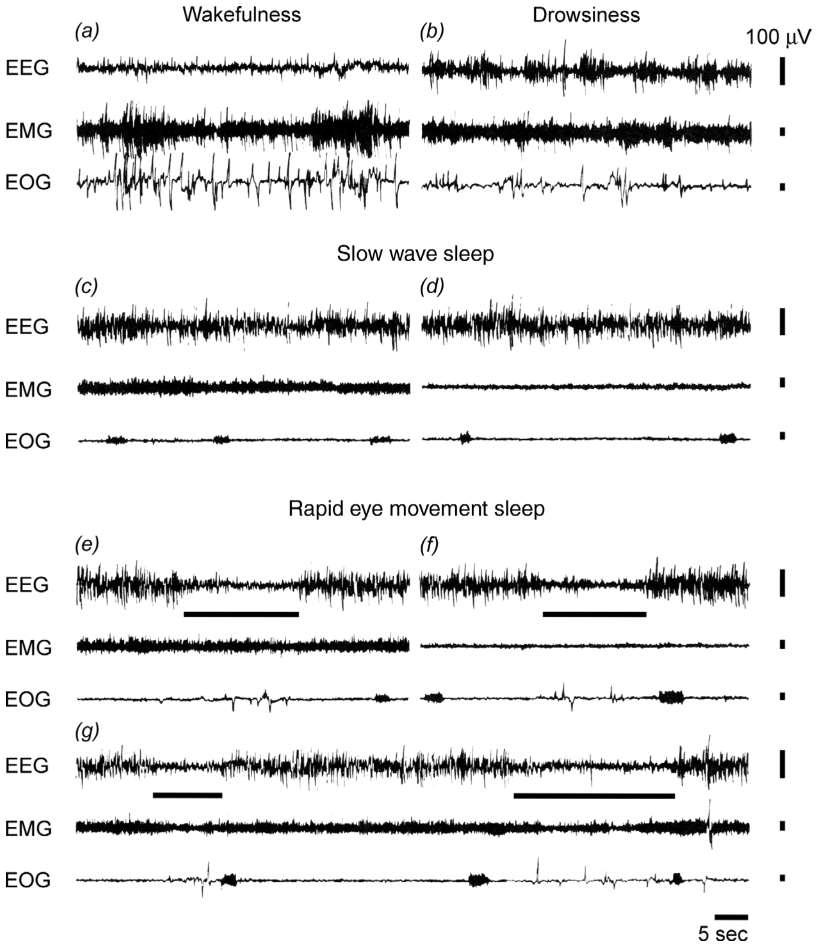

Figure 7.2 Electroencephalogram (EEG), electromyogram (EMG), and electrooculogram (EOG) recordings of wakefulness (*a*), drowsiness (*b*), slow-wave sleep (SWS) (*c–d*), and rapid eye movement (REM) sleep (*e–g*) in an emperor penguin (*Aptenodytes forsteri*). During drowsiness, the EEG alternates rapidly between a pattern typical of wakefulness and that typical of SWS. Slow-wave sleep can occur with high (*c*) or low (*d*) tonic EMG activity. The intermittent increases in EOG amplitude occurring during SWS reflect brief, rapid oscillations of the eyes. Transitions between SWS and REM sleep are shown in (*e–g*); the horizontal black bars mark REM sleep. As with SWS, REM sleep can occur with high (*e*) or low (*f*) tonic EMG activity. In rare cases, however, EMG activity may decrease during episodes of REM sleep (*g*). The states depicted in the penguin are typical of those reported in other bird species. Modified from Buchet *et al.* (1986).

SWS may perform similar functions in homeotherms (Rattenborg *et al.*, 2009).

As in therian mammals, avian REM sleep is characterized by low-amplitude, high-frequency EEG activity similar to that occurring during wakefulness (Figure 7.2). Unlike mammals, however, a hippocampal theta rhythm has not been recorded during avian REM sleep (van Twyver and Allison, 1972). Recordings of brain-stem neuronal activity similar to those performed in the eutherian mammals, echidnas, and turtles, have not been performed in birds. Nonetheless, rapid eye movements and occasional twitching occur during avian REM sleep. The possible equivalent of PGO waves have been reported in the optic tectum in association with rapid eye movements (Sugihara and Gotoh, 1973), although this feature of mammalian REM sleep has not been studied extensively in birds. Although nuchal EMG recordings rarely show reduced amplitude during REM sleep, behavioral signs of reduced tone, including head drooping, are often observed. Interestingly, nuchal hypotonia and atonia are observed in geese only when they support the head on their back (Dewasmes *et al.*, 1985). This suggests that birds actively maintain partial nuchal muscle tone during REM sleep in an attempt to support the head. As in mammals, thermoregulatory responses, such as shivering and feather raising, are reduced during REM sleep when compared to SWS and wakefulness (Heller *et al.*, 1983). Unlike mammals, episodes of REM sleep are short, typically lasting less than ten seconds (e.g., Martinez-Gonzalez *et al.*, 2008). The short duration does not appear to be an adaptation to prevent falling from a perch, because REM sleep episodes are also short in birds that sleep on the ground (Dewasmes *et al.*, 1985). In pigeons (*Columba livia*), the duration of REM sleep episodes and overall time spent in REM sleep increases across the night (Martinez-Gonzalez *et al.*, 2008), a pattern similar to that observed in some mammals. The overall amount of time spent in REM sleep appears to be lower in birds, when compared to mammals (Lesku *et al.*, 2009), although recent studies suggest that songbirds may have more REM sleep than previously recognized (Low *et al.*, 2008; Rattenborg *et al.*, 2004). The time spent in REM sleep increases following 8 and 24 hours of sleep deprivation enforced via gentle handling (Martinez-Gonzalez *et al.*, 2008; Tobler and Borbély, 1988, respectively), and after long-term sleep restriction enforced via the disk-over-water method (Newman *et al.*, 2008). Although pigeons failed to develop the sleep deprivation syndrome observed in rats sleep deprived via the disk-over-water method (Rechtschaffen and Bergmann, 2002), this method was less effective in reducing sleep, particularly REM sleep, in pigeons (Newman *et al.*, 2008). Consequently, it remains unclear whether birds respond to long-term sleep loss in the same manner as rats. Collectively, comparative work in birds indicates that they exhibit sleep states remarkably similar to those in therian mammals. Nonetheless, potentially informative differences include the absence of a hippocampal theta rhythm and the short duration of REM sleep episodes. Functional theories for the evolution of REM sleep that account for these differences between birds and mammals are more likely to explain the core purpose of this state, rather than mammal-specific aspects of REM sleep.

Convergent evolution of REM sleep in mammals and birds

Given the presence of unequivocal REM sleep in birds, and its apparent absence in non-avian reptiles, amphibians, and fish, the most parsimonious evolutionary explanation for the taxonomic distribution of REM sleep is that it evolved independently in birds and mammals (Figure 7.3). Interestingly, SWS also seems to have evolved independently in mammals and birds, although sleep in reptiles, and possibly other vertebrates, may reflect a precursor state that lacks the high-amplitude, low-frequency EEG activity characteristic of SWS (Rattenborg, 2006, 2007). This convergence in sleep states may be interrelated with other trait(s) that among vertebrates are only shared by mammals and birds. Interestingly, in addition to evolving similar sleep states, mammals and birds also independently evolved

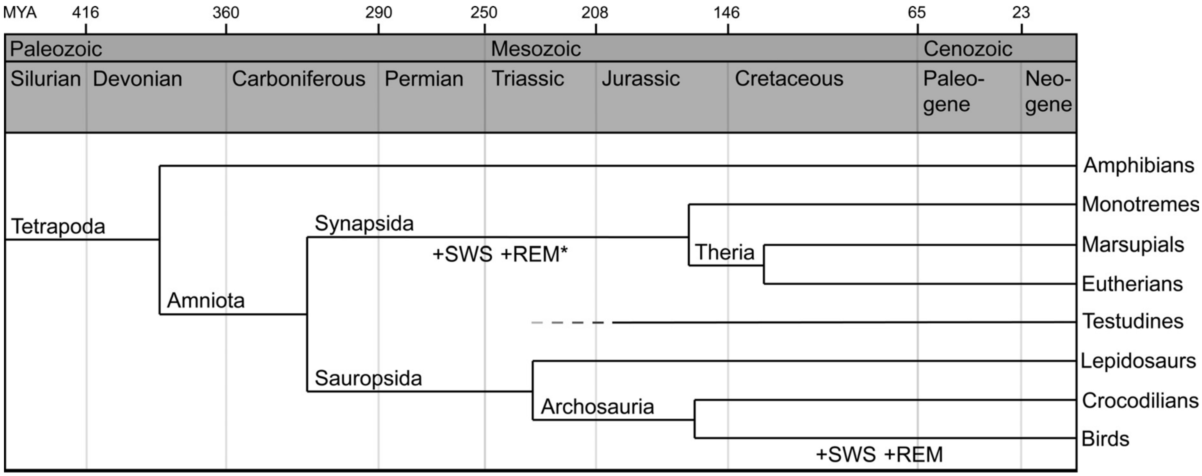

Figure 7.3 A cladogram for tetrapods showing the convergent evolution of rapid eye movement (REM) sleep and slow-wave sleep (SWS) in mammals and birds. The origin of REM sleep and SWS are depicted as +REM and +SWS, respectively. The asterisk after +REM in the mammalian lineage indicates uncertainty over when REM sleep-related cortical activation evolved. Based on evidence for REM sleep-related brain-stem activity in monotremes, this component of REM sleep was probably present in the common ancestor to all mammals. However, the absence of REM sleep-related cortical activation in monotremes suggests that this trait evolved after Prototheria diverged from the mammalian lineage. Alternatively, neuroanatomical data suggest that monotremes may have lost REM sleep-related cortical activation. Based on the presence of high-amplitude, slow waves in the EEG, SWS apparently also originated independently (+SWS) in mammals and birds. Time (millions of years ago, MYA) is given at the top of the plot above geological era (dark gray) and period (light gray). The phylogenetic relationships are well established for all groups except testudines (turtles). As a result, the root of this lineage is not depicted. Lepidosaurs include lizards and snakes, and the tuatara. Estimates of divergence times are from Warren *et al.* (2008).

large (relative to body size), heavily interconnected brains capable of performing complex cognitive processes (Jarvis *et al.*, 2005; Medina and Abellán, 2009). The known taxonomic distribution of REM sleep and SWS is consistent with the notion that both states are involved in maintaining brain function in animals with such brains (Rattenborg, 2006; Rattenborg *et al.*, 2009), although other examples of the coevolution of large, heavily interconnected brains and mammalian-like sleep states would certainly strengthen this argument. Alternatively, REM sleep and SWS might perform conserved sleep functions, but mammals and birds simply differ in the manner in which such states manifest electrophysiologically. The EEG correlates of sleep in mammals and birds could either reflect functionless epiphenomena resulting from large, heavily interconnected brains, or different mechanisms for performing a conserved sleep function. Indeed, genetic work in *Drosophila melanogaster*, suggests that some sleep mechanisms and functions may be highly conserved (Mignot, 2008; Cirelli and Bushey, 2008). Nonetheless, despite the conserved nature of genetic correlates of sleep, the EEG traits, and underlying neurophysiology that characterize sleep and its sub-states in mammals and birds may perform secondarily evolved sleep functions not found in animals lacking REM sleep and SWS (Rattenborg *et al.*, 2009).

Evolutionary loss of REM sleep

Identifying the type of animals in which REM sleep evolved may yield clues to the function of this state through revealing associated traits, such as heavily interconnected brains in mammals and birds. Conversely, the evolutionary loss of REM sleep may also be informative if it occurs concurrent with the loss of other traits. Traits that disappear along with REM sleep may be functionally related to REM sleep, especially if they also coevolved with REM sleep in mammals and birds in the first place. It is also conceivable that animals that lose REM sleep retain traits that depend on REM sleep, but evolve novel mechanisms to compensate for this loss. In this case, revealing the nature of such mechanisms may inform our understanding of REM sleep. Although the evidence remains somewhat equivocal, odontocete cetaceans (dolphins and porpoises) may have lost REM sleep-related cortical activation, a trait thought to be involved in the function of REM sleep in other therian mammals.

Life in an aquatic environment apparently contributed to the evolution of modified forms of SWS and REM sleep in cetaceans (Lyamin *et al.*, 2008). Unlike terrestrial mammals, where SWS occurs simultaneously in both hemispheres, cetaceans primarily engage in unihemispheric SWS (USWS), an unusual state in which one cerebral hemisphere shows EEG activity indicative of SWS while the other shows a waking pattern. During USWS, the eye contralateral to the awake hemisphere is usually open, whereas the eye contralateral to the sleeping hemisphere is usually closed. Cetaceans swim and surface to breathe during USWS, and seem to visually monitor their environment with the open eye during this state. In addition to this specialized form of SWS, REM sleep also seems to have been modified to suit life in an aquatic environment. Most electrophysiological studies of sleep in odontocetes failed to detect unequivocal signs of REM sleep. Although an early study reported a single episode of REM sleep with cortical EEG activation in a pilot whale (*Globicephala scammoni*, an odontocete), subsequent studies were unable to replicate this finding in four other species. Efforts to detect REM sleep were most intense in the bottlenose dolphin, where recordings from both lateral geniculate bodies and hippocampi failed to reveal PGO spikes or a hippocampal theta rhythm, respectively, during wakefulness or sleep. The absence of traditional REM sleep-related traits does not necessarily indicate that cetaceans are completely devoid of an REM sleep-like state. Interestingly, in contrast to studies employing electrophysiological recordings of tethered animals, behavioral studies of untethered captive animals revealed rare head, body, and eye-lid twitching while the animal rested on the bottom of the pool or swam slowly, in both odontocetes and a single young mysticete (balleen) gray whale (*Eschrichtius robustus*). Penile erections have also been observed in sleeping cetaceans. In the Commerson's dolphin (*Cephalorhynchus commersonii*), erections and twitching were temporally associated. Although suggestive of a brief REM sleep-like state, the diagnostic utility of these phenomena is limited by the finding that twitches and penile erections also occur during wakefulness, and twitching can occur during sleep onset and in SWS in terrestrial mammals (Lyamin *et al.*, 2008). Collectively, the electrophysiological and behavioral studies of captive cetaceans suggest that if REM sleep exists in this group, it is greatly reduced when compared to other therian mammals and may occur in a modified manner that does not necessarily include cortical activation.

Manger and colleagues have proposed that these modifications to REM sleep and the almost exclusive reliance on USWS both reflect adaptations aimed at reducing heat loss in an aquatic environment, a significant problem for "warm-blooded" mammals. Unihemispheric SWS allows cetaceans to generate heat via swimming, and the marked reduction or absence of REM sleep prevents the loss of heat that would occur as a result of the immobility and reduced thermoregulation that accompanies REM sleep in terrestrial therian mammals (Lyamin *et al.*, 2008; Manger, 2006). The finding that cetaceans evolved USWS, rather than dispensing with SWS altogether (a more thermogenic alternative than USWS), indicates that SWS must perform an important function, presumably for the cortex itself.

The absence of REM sleep-related cortical activation, or REM sleep altogether, in cetaceans appears to be a derived loss of this trait, because REM sleep has been detected in all other therian mammals studied. Although the potential loss of REM sleep-related cortical activation in cetaceans suggests that it is evolutionarily possible to dispense with this trait under certain ecological circumstances, it does not necessarily challenge the importance of REM sleep in the lives of other mammals. Indeed, the evolutionary preservation of REM sleep with cortical activation in all other therian mammals, despite comparative evidence indicating that REM sleep may be a particularly dangerous state (see below), indicates that it must perform an important function. Otherwise, one would expect the loss of REM sleep to be more common.

Evolutionary determinants of REM sleep duration

A potentially revealing approach to unraveling the functions of REM sleep is to explain why some species spend a great deal of time in REM sleep and others only very little. If we assume that such across-species (or interspecific) variation reflects underlying differences in the need for REM sleep, then identifying the factors responsible for maintaining that variation should provide clues to the function of REM sleep. Although such comparative analyses typically address both REM sleep and SWS, here we only review the more relevant relationships bearing on the functions of REM sleep (see Lesku *et al.*, 2009 for a complete review). Furthermore, our discussion is restricted to recent studies that employed modern phylogenetic comparative methods to control for pseudoreplication resulting from the inclusion of closely related species with similar sleep traits, a standard in evolutionary biology that only recently has been applied to sleep research (Lesku *et al.*, 2009).

The degree of maturity at birth has consistently been the strongest predictor of the time spent in REM sleep and the allocation of time asleep to REM sleep (or percentage of REM sleep). Altricial species, those that are born largely immobile and rely entirely on their parents for nourishment, warmth, and protection have more REM sleep as adults than more precocial species. This relationship is in agreement with early EEG work by Jouvet-Mounier *et al.* (1970), which shows that the rat and cat, as altricial species, have more REM sleep throughout their life than the precocial guinea pig (Figure 7.4). These findings collectively suggest that REM sleep is important for the early development of the central nervous system (Shaffery *et al.*, 2002), although it is unclear why this difference persists into adulthood (Siegel, 2011).

Increasing evidence indicates that sleep, REM sleep included, is important for memory processing and plasticity (Stickgold and Walker, 2007). What comparative evidence exists to support this hypothesis? If enhancing cognitive performance is a general function of REM sleep across mammals, then one might expect species possessing greater cognitive abilities

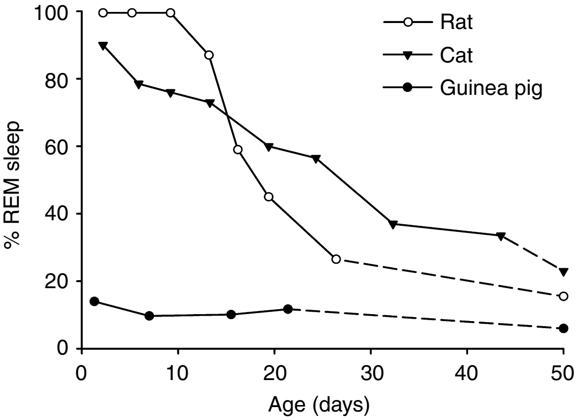

Figure 7.4 Changes in the percentage of total sleep time devoted to rapid eye movement (% REM) sleep across early development in the rat, cat, and guinea pig. In the altricial rat and cat, REM sleep constitutes most of total sleep time and decreases to levels close to that of adults approximately one month after birth. Conversely, % REM sleep in the precocial guinea pig is relatively stable over early ontogeny and into adulthood. Note, however, that even as adults, altricial species have higher %REM sleep than more precocial species. Reprinted Jouvet-Mounier *et al.* (1970).

to engage in more REM sleep. Encephalization is a possible measure of interspecific intelligence as it estimates the degree to which a species' brain is bigger or smaller than that expected for its body size. Encephalization may not be the most precise variable with which to assess interspecific support for sleep-dependent memory consolidation, it is nevertheless readily obtainable for the species for which EEG-based sleep data are available. Although encephalization is not a strong predictor of the time spent in REM sleep, species with greater encephalization allocate a higher percentage of time asleep to REM sleep (Lesku *et al.*, 2006, 2009), as expected if REM sleep is involved in memory processing.

Not all mammals studied were included in the above analyses. Monotremes were excluded because it is unclear how to quantify REM sleep time in animals that exhibit a heterogeneous sleep state with aspects of REM sleep and SWS occurring concurrently (see section on Monotremes, above). Cetaceans were also excluded from these phylogenetic analyses, because it is not clear how to express the time spent asleep in these unihemispherically sleeping animals (see section on Evolutionary loss of REM sleep, above). Nonetheless, they may have bearing on the relationship between encephalization and percentage REM sleep reported above. In addition to engaging primarily in USWS, these animals also apparently lack cortical signs of REM sleep (Lyamin *et al.*, 2008). This apparent loss of REM sleep is surprising as some cetaceans reach a level of encephalization shared by some anthropoid primates (Marino *et al.*, 2008). Thus, if REM sleep is important for information processing, then cetaceans have either found a mechanism other than REM sleep to support their advanced cognition or, as suggested by Manger (2006), cetaceans are not as intelligent as previously thought (but see Marino *et al.*, 2008).

Given the marked reduction or absence of REM sleep in cetaceans, the time spent in REM sleep may be constrained by additional ecological factors, such as the risk of predation. Indeed, species sleeping in more open locations, and more herbivorous species, engage in less REM sleep (both total time and as a percentage of sleep time) relative to their more secure-sleeping and carnivorous counterparts (Lesku *et al.*, 2006), suggesting that REM sleep is a particularly vulnerable sleep state that is selectively reduced when risk is elevated. This comparative result is mirrored in laboratory studies where REM sleep is disproportionately reduced following simulated predatory encounters (Lesku *et al.*, 2008). Presumably, a trade-off exists between the biological need for REM sleep and ecological factors selecting against REM sleep that accounts for this relationship, as well as the preservation of at least some REM sleep in most mammals.

Although common in other biological disciplines, trade-offs of this sort have not been taken into consideration by sleep researchers. Indeed, much of the variability in sleep times observed in mammals may reflect a combination of species-specific differences in the need for sleep and trade-offs between the benefit and costs of engaging in a particular state. For instance, although two species may have the same biological need for sleep, the cost–benefit ratio of sleeping may differ between the two, resulting in differences in sleep time. Such trade-offs could occur under both evolutionary and ecological time scales, and may vary seasonally within a species in response to changing ecological demands (Rattenborg *et al.*, 2004). Ultimately, it would be informative to determine the short-term costs (e.g., energy expenditure, memory, vigilance, etc.) and potential long-term costs (e.g., longevity, fecundity, etc.) of engaging in more or less of a particular sleep state. The manner in which such trade-offs occur, and their influence on brain function and behavior, may provide insight into the function of sleep. Finally, trade-offs may be best examined in animals living in their natural environment, rather than the laboratory environment (Horne, 2009; Siegel, 2009), a promising approach recently made feasible by the development of techniques for recording sleep in animals living in the ecological context in which sleep evolved (Rattenborg *et al.*, 2008).

Conclusion

Our interpretation of the available research bearing on the evolution of REM sleep is subject to several caveats, and therefore remains tentative. A fundamental caveat of all comparative studies that attempt to trace the evolution of traits that do not fossilize, such as sleep, is that extant representatives of a taxonomic group have undergone millions of years of evolution since their group first appeared, and therefore might not represent the sleep patterns of their ancestors. Other caveats relate to the limited scope of the available data. Many critical points in our understanding are based only on a few species, either because certain taxonomic groups have been poorly studied, or because only a few species are available for study, as is the case in monotremes.

Moreover, certain potentially important defining traits of REM sleep, such as brain-stem activity, have only been examined in a small number of species. As a result, it remains unclear whether these results generalize to an entire taxonomic group. In some cases, the results from the same taxonomic group, or even species, reveal different results, or different interpretations of comparable results. This has been particularly true in fish, amphibians, and non-avian reptiles (Hartse, 1994; Rattenborg, 2007), as well as monotremes. Historically, comparative studies have been based on data obtained from animals sleeping in an unnatural laboratory environment. Given that REM sleep in therian mammals is particularly sensitive to changes in temperature, predation risk, etc., the laboratory environment may influence the amount of time spent in this state, or could even account for reports of its absence in certain taxonomic groups, such as reptiles. Our confidence in concluding that a particular taxonomic group exhibits REM sleep diminishes as fewer therian mammal REM sleep-related traits are identified. This may reflect the simple fact that not all traits exist in a particular taxonomic group and/or that they do not manifest in the same manner, perhaps due to differences in neuroanatomy. Moreover, some traits may exist, but evade detection, either because we are unsure where to look for them or because recording them is technically challenging, as is the case in insects. Some traits that typically occur during REM sleep in therian mammals, such as twitching, may also occur during other sleep states, and therefore are not diagnostic of REM sleep. Conversely, the absence of twitching does not necessarily indicate an absence of REM sleep-related brain-stem activity, as demonstrated in the echidna, where REM sleep-like brain-stem activity occurred in the absence of twitching (Siegel *et al.*, 1996). Finally, our understanding of the evolution of REM sleep also depends on whether a sleep trait is viewed as ancestral or a derived modification of a pre-existing sleep trait. This is particularly problematic in groups thought to represent a pivotal point in evolution. For instance, the lack of cortical activation in monotremes may reflect the sleep state present in the common ancestor to all mammals or a derived modification of REM sleep, as suggested by neuroanatomical data.

Keeping in mind each caveat, the available evidence suggests the following evolutionary scenario for REM sleep. Given the lack of unequivocal evidence for REM sleep in fish, amphibians, and non-avian reptiles, signs of REM sleep first appeared in the common ancestor to monotreme, marsupial, and eutherian mammals. If we assume that the sleep patterns exhibited by extant monotremes have changed little since the monotreme lineage diverged from therian mammals, then the ancestor to all mammals presumably exhibited a heterogeneous sleep state characterized by REM sleep-related activity in the brain stem occurring concurrently with cortical SWS. Alternatively, neuroanatomical data raises the possibility that REM sleep-related cortical activation was present in the common ancestor to all mammals, but monotremes subsequently lost this trait prior to diverging into echidnas and platypuses. Regardless of when REM sleep-related cortical activation evolved, REM sleep-like brain-stem activity was apparently present in the ancestors to all mammals. Furthermore, the absence of REM sleep-like brain-stem activity in a single study of sleeping turtles suggests that this trait evolved after amniotes split into synapsids (the ancestors to mammals) and sauropsids (the ancestors to reptiles, including birds), although more species clearly need to be studied to resolve the evolution of this trait.

The diversification of Mammalia was associated with the evolution of marked interspecific variation in the time spent in REM sleep. Comparative studies have shown that REM sleep in adult mammals is higher in species altricial at birth and those with greater encephalization as adults, both suggesting a neurologically based role for this state. Ecological factors such as the risk of predation during sleep also influenced the amount of REM sleep, with mammals experiencing greater risk engaging in less REM sleep. Nonetheless, despite the inherent risk of predation associated with REM sleep, this state was retained in all, except perhaps one group of, mammals, testament to the biological importance of this state. Only in cetaceans was REM sleep greatly reduced or completely lost, a modification in sleep that along with USWS may be specialized adaptations for life in the sea (Lyamin *et al.*, 2008).

In addition to mammals, REM sleep with EEG activation also evolved in the common ancestor to extant birds. Given the absence of REM sleep in crocodilians, the closest living relatives to birds, as well as other reptiles and amphibians, REM sleep apparently evolved independently in the respective ancestors of birds and mammals. The convergent evolution of REM sleep (and SWS) in mammals and birds suggests that the efficacy of certain biological traits unique to these taxonomic groups depends on these sleep states. For instance, the convergent evolution of similar sleep states may be mechanistically and functionally linked to the associated convergent evolution of large, heavily interconnected brains capable of complex cognition in mammals and birds, although the role of other interrelated traits, such as homeothermy, can not be ruled out (Rattenborg *et al*., 2009).

Sleep, in general, appears to be a highly conserved trait present in all animals investigated. This suggests that sleep likely serves a basic, perhaps cellular, function in all animals. However, it is also likely that once sleep evolved, other functions became dependent on sleep. The relative importance of such secondarily evolved functions may vary across taxonomic groups. Consequently, our understanding of sleep in humans will be incomplete until we determine both the initial cellular function of sleep and potential secondarily evolved functions associated with the changes in brain activity that characterize SWS and REM sleep. Here, additional comparative work on sleep in vertebrates may be particularly informative. Notably, efforts to determine why only mammals and birds exhibit SWS and REM sleep may reveal overriding principles that might otherwise remain obscure through a strictly mammal-focused research approach.

References

Affanni, J. M., Cervino, C. O. & Marcos, H. J. (2001) Absence of penile erections during paradoxical sleep. Peculiar penile events during wakefulness and slow wave sleep in the armadillo. *J Sleep Res* **10**: 219–28.

Allison, T., van Twyver, H. & Goff, W. R. (1972) Electrophysiological studies of the echidna, *Tachyglossus aculeatus*. I. Waking and sleep. *Arch Ital Biol*, **110**: 145–84.

Buchet, C., Dewasmes, G. & Le Maho, Y. (1986) An electrophysiological and behavioral study of sleep in emperor penguins under natural ambient conditions. *Physiol Behav* **38**: 331–5.

Cirelli, C. & Bushey, D. (2008) Sleep and wakefulness in *Drosophila melanogaster*. *Ann N Y Acad Sci* **1129**: 323–9.

Cirelli, C. & Tononi, G. (2008) Is sleep essential? *PLoS Biology* **6**: e216.

Dewasmes, G., Cohen-Adad, F., Koubi, H. & Le Maho, Y. (1985) Polygraphic and behavioral study of sleep in geese: existence of nuchal atonia during paradoxical sleep. *Physiol Behav* **35**: 67–73.

Eiland, M. M., Lyamin, O. I. & Siegel, J. M. (2001) State-related discharge of neurons in the brainstem of freely moving box turtles, *Terrapene carolina major*. *Arch Ital Biol* **139**: 23–36.

Hartse, K. M. (1994) Sleep in insects and nonmammalian vertebrates. In *Principles and Practice of Sleep Medicine*, 2nd edn. eds. M. H. Kryger, T. Roth & W. C. Dement. Philadelphia: W. B. Saunders, pp. 95–104.

Heller, H. C., Graf, R. & Rautenberg, W. (1983) Circadian and arousal state influences on thermoregulation in the pigeon. *Am J Physiol* **245**: R321–8.

Horne, J. (2009) REM sleep, energy balance and 'optimal foraging'. *Neurosci Biobehav Rev* **33**: 466–74.

Jarvis, E. D., Güntürkün, O., Bruce, L. *et al.* (2005) Avian brains and a new understanding of vertebrate brain evolution. *Nat Rev Neurosci* **6**: 151–9.

Jouvet, M. (1962) Recherches sur les structures nerveuses et les mechanismes responsables des differentes phases du sommeil physiologique. *Arch Ital Biol* **100**: 125–206.

Jouvet-Mounier, D., Astic, L. & Lacote, D. (1970) Ontogenesis of the states of sleep in rat, cat, and guinea pig during the first postnatal month. *Dev Psychobiol* **2**: 216–39.

Lesku, J. A., Roth, T. C., 2nd, Amlaner, C. J. & Lima, S. L. (2006) A phylogenetic analysis of sleep architecture in mammals: the integration of anatomy, physiology, and ecology. *Amer Nat* **168**: 441–53.

Lesku, J. A., Bark, R. J., Martinez-Gonzalez, D. *et al.* (2008) Predator-induced plasticity in sleep architecture in wild-caught Norway rats (*Rattus norvegicus*). *Behavi Brain Res* **189**: 298–305.

Lesku, J. A., Roth, T. C., Rattenborg, N. C., Amlaner, C. J. & Lima, S. L. (2009) History and future of comparative analyses in sleep research. *Neurosci Biobehavi Rev* **33**: 1024–36.

Low, P. S., Shank, S. S., Sejnowski, T. J. & Margoliash, D. (2008) Mammalian-like features of sleep structure in zebra finches. *Proc Nat Acad Sci USA* **105**: 9081–6.

Lyamin, O. I., Manger, P. R., Ridgway, S. H., Mukhametov, L. M. & Siegel, J. M. (2008) Cetacean sleep: an unusual form of mammalian sleep. *Neurosci Biobeh Rev* **32**: 1451–84.

Lyson, T. & Gilbert, S. F. (2009) Turtles all the way down: loggerheads at the root of the chelonian tree. *Evol Dev* **11**:133–5.

Manger, P. R. (2006) An examination of cetacean brain structure with a novel hypothesis correlating thermogenesis to the evolution of a big brain. *Biol Rev* **81**: 293–338.

Manger, P. R., Fahringer, H. M., Pettigrew, J. D. & Siegel, J. M. (2002) The distribution and morphological characteristics of cholinergic cells in the brain of monotremes as revealed by ChAT immunohistochemistry. *Brain Behav Evol* **60**: 275–97.

Marino, L., Butti, C., Connor, R. C. *et al.* (2008) A claim in search of evidence: reply to Manger's thermogenesis hypothesis of cetacean brain structure. *Biol Rev* **83**: 417–40.

Martinez-Gonzalez, D., Lesku, J. A. & Rattenborg, N. C. (2008) Increased EEG spectral power density during sleep following short-term sleep deprivation in pigeons (*Columba livia*): evidence for avian sleep homeostasis. *J Sleep Res* **17**: 140–53.

Medina, L. & Abellán, A. (2009) Development and evolution of the pallium. *Semin Cell Dev Biol* **20**: 698–711.

Mignot, E. (2008) Why we sleep: the temporal organization of recovery. *PLoS Biology* **6**: e106.

Newman, S. M., Paletz, E. M., Rattenborg, N. C., Obermeyer, W. H. & Benca, R. M. (2008) Sleep deprivation in the pigeon (*Columba livia*) using the disk-over-water method. *Physiol Behav* **93**: 50–8.

Nicol, S. C., Andersen, N. A., Phillips, N. H. & Berger, R. J. (2000) The echidna manifests typical characteristics of rapid eye movement sleep. *Neurosci Lett* **283**: 49–52.

Ordoñez, G. R., Hillier, L. W., Warren, W. C. (2008) Loss of genes implicated in gastric function during platypus evolution. *Genome Biol* **9**: R81.

Parmeggiani, P. L. (2003) Thermoregulation and sleep. *Front Biosci* **8**: s557–67.

Rattenborg, N. C. (2006) Evolution of slow-wave sleep and palliopallial connectivity in mammals and birds: a hypothesis. *Brain Res Bull* **69**: 20–9.

Rattenborg, N. C. (2007) Response to commentary on evolution of slow-wave sleep and palliopallial connectivity in mammals and birds: a hypothesis. *Brain Res Bull* **72**: 187–93.

Rattenborg, N. C., Mandt, B. H., Obermeyer, W. H. *et al.* (2004) Migratory sleeplessness in the white-crowned sparrow (*Zonotrichia leucophrys gambelii*). *PLoS Biology* **2**: 924–36.

Rattenborg, N. C., Martinez-Gonzalez, D. & Lesku, J. A. (2009) Avian sleep homeostasis: convergent evolution of complex brains, cognition and sleep functions in mammals and birds. *Neurosci Biobehav Rev* **33**: 253–70.

Rattenborg, N. C., Voirin, B., Vyssotski, A. L. *et al.* (2008) Sleeping outside the box: electroencephalographic measures of sleep in sloths inhabiting a rainforest. *Biol Lett* **4**: 402–5.

Rechtschaffen, A. & Bergmann, B. M. (2002) Sleep deprivation in the rat: an update of the 1989 paper. *Sleep* **25**: 18–24.

Sereno, P. C. (1999) The evolution of dinosaurs. *Science* **284**: 2137–47.

Shaffery, J. P., Sinton, C. M., Bissette, G., Roffwarg, H. P. & Marks, G. A. (2002) Rapid eye movement sleep deprivation modifies expression of long-term potentiation in visual cortex of immature rats. *Neuroscience* **110**:431–43.

Siegel, J. M. (2009) Sleep viewed as a state of adaptive inactivity. *Nat Rev Neurosci*, **10**: 747–53.

Siegel, J. M. (2011) REM sleep. In *Principles and Practice of Sleep Medicine*, 5th edn. eds. M. H. Kryger, T. Roth & W. C. Dement. Philadelphia: W. B. Saunders, pp. 92–111.

Siegel, J. M., Manger, P. R., Nienhuis, R., Fahringer, H. M. & Pettigrew, J. D. (1996) The echidna *Tachyglossus aculeatus* combines REM and non-REM aspects in a single sleep state: implications for the evolution of sleep. *J Neurosci* **16**: 3500–6.

Siegel, J. M., Manger, P. R., Nienhuis, R. *et al.* (1999) Sleep in the platypus. *Neuroscience* **91**:391–400.

Stickgold, R. & Walker, M. P. (2007) Sleep-dependent memory consolidation and reconsolidation. *Sleep Med* **8**: 331–43.

Sugihara, K. & Gotoh, J. (1973) Depth-electroencephalograms of chickens in wakefulness and sleep. *Jpn J Physiol* **23**:371–9.

Tobler, I. (2011) Phylogeny of sleep regulation. In *Principles and Practice of Sleep Medicine*, 5th edn. eds. M. H. Kryger, T. Roth & W.C. Dement. Philadelphia: W. B. Saunders, pp. 112–25.

Tobler, I. & Borbély, A. A. (1988) Sleep and EEG spectra in the pigeon (*Columba livia*) under baseline conditions and after sleep-deprivation. *J Comp Physiol, A* **163**: 729–38.

van Twyver, H. & Allison, T. (1972) A polygraphic and behavioral study of sleep in the pigeon (*Columba livia*). *Exp Neurol* **35**: 138–53.

Warren, W. C., Hillier, L. W., Marshall Graves, J. A., Birney, E., Ponting, C. P. *et al.* (2008) Genome analysis of the platypus reveals unique signatures of evolution. *Nature* **453**: 175–83.