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Siegel, J.M. The evolution of REM sleep. In Handbook of Behavioral State Control., Lydic, R and Baghdoyan (Eds.), pp 87-100, CRC Press, Boca Raton, 1999.

The evolution of REM sleep

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Supported by the Medical Research Service of the Department of Veterans Affairs and USPHS grant NS32819

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INTRODUCTION

An understanding of the nature, amount and distribution of REM sleep across the animal kingdom allows one to form hypotheses about its evolutionary history and function. Attributes of sleep common to several branches of the evolutionary tree are likely to have been present in the common ancestor. Conversely, attributes present in only one branch are likely to have arisen in that branch.

Most studies of sleep have been conducted in humans, with lesser numbers in "standard" laboratory animals such as the rat, rabbit and dog. Relatively few studies have been conducted of the more than 4000 other mammalian species. However, those studies that have been undertaken clearly show that REM sleep amounts vary enormously across the animal kingdom. REM sleep has been identified in birds, but very few avian species have been investigated. [3] The number of studies of amphibian and reptilian sleep is miniscule, with few such studies using rigorous electrophysiological and behavioral indices.

DEFINITION OF REM SLEEP

The criteria for defining a state as "sleep" or as REM sleep can become a significant issue in interpreting data from animal studies. Our understanding of the nature of sleep states is largely based on studies of the cat. In this species, we know the EEG changes correlated with sleep and their developmental history. We also know the basic parameters of the changes in neuronal activity in the cortex responsible for the EEG changes during the sleep cycle. We know much about the thalamic neurons generating cortical rhythmicity. [42] NonREM sleep promoting neurons in the basal forebrain have been identified, as have wake inducing systems in the posterior hypothalamus and brainstem. [23, 28, 35] Finally, a system of neurons generating the EEG, eye movement, twitches and underlying muscle atonia of REM sleep have been identified in the brainstem (reviewed in [40]). This system utilizes noradrenergic and serotonergic REM sleep-off neurons, GABAergic, cholinergic, glycinergic and glutamatergic REM sleep-on cells as well as other neurons. Cells that are active in both waking and REM sleep are important in generating some of the phasic motor phenomena of both of these states. The driving force responsible for the triggering of REM sleep and for controlling its duration is completely unknown.

Given what we now know about REM sleep, how can we go about defining it in newly examined animals? Ideally and ultimately, one needs to know the activity of all of the cell groups listed above to say that a state has all the characteristics of REM sleep in the cat. If a previously unexamined species were found to have two states of sleep, one with phasic motor activity and one without, one would want to know if the other aspects of REM sleep, documented in the cat were present. Specifically, are there noradrenergic and serotonergic REM sleep-off cells and GABAergic, glutamatergic and cholinergic REM sleep-on cells? Are there brainstem pre-motor cells firing in bursts during REM sleep? Is there active inhibition of motoneurons during this state? Are there ascending glutamatergic and cholinergic systems responsible for the low voltage EEG activity of this state?

These relatively rigorous criteria would provide a useful description of the commonalties in the neuronal activity features that characterize

REM sleep across the animal kingdom. However, we must appreciate that today these key features of REM sleep have been documented only in the adult cat. We do not know if the same pattern of REM sleep-on, REM sleep-off and REM-waking active cells is present in humans during REM sleep. We do not know if the neurochemistry of these systems is the same in all species. The key anatomical structures responsible for REM sleep control in the cat are distributed differently in the human, rat and other species. [4, 22, 26, 31, 39] Although these cell groups are present in other mammalian species, they are also present in modified form in fish and amphibia. [19, 20, 24, 46, 49, 50] Moreover these cell groups are present in neonatal rats and cats even though "REM sleep" characteristics are very different at these ages. Chemical microinjection studies in the rat have yet to clearly duplicate the rapid induction of REM sleep and muscle atonia reported more than 30 years ago in the cat and repeatedly confirmed by others. [14] Serotonin depletion in the cat produces insomnia, but has no such effect in the rat. [36, 37]

In neonatal humans, [18, 43] cats [29] and rats [13] the EEG voltage reduction that characterizes REM sleep in the adult cat, rat and human does not occur. However the phasic motor activation (twitching) that characterizes REM sleep in the adult animal is present. Since the amplitude of the twitching is more intense in neonates than in the adult, the motor inhibition is either less effective or the intensity of the phasic excitation is greater in newborns. Are these differences in motor activation and inhibition and EEG changes caused by the activity of aminergic, cholinergic, GABAergic and glutamatergic cells? Are they a result of incomplete myelination of the axons of these systems? Are they due to immaturity of postsynaptic receptors? Are they due to neuronal differentiation and synaptogenesis? Is some combination of the above critical and if so, what is the relative role of these changes and other changes not itemized?

I mention these points because of their relevance to the issue of state definition in non-laboratory species. We can observe a developmental continuity between "active sleep" in the neonate and REM sleep in the adult. The neonatal state of twitching gradually acquires the EEG voltage reduction and muscle atonia of REM sleep. This continuity makes it easy to accept that the neonatal "active sleep" state is closely related to the state of REM sleep (also known as paradoxical sleep) seen in the adult.

The behavioral similarity of the REM sleep state in the human and cat makes it reasonable to hypothesize that the neuronal activity changes known to underlie the state of REM sleep in the cat are occurring in the human. However, minor and major differences might be found when it becomes possible to monitor the precise behavior of chemically identified cell groups in the human. While rapid eye movements were the feature of REM sleep that gave this state its most mellifluous name, animals can have few or no eye movements in waking and REM sleep, yet still have a state of phasic motor activity (accompanied by low voltage EEG) within sleep. [1]

Both active sleep in the neonate and REM sleep in the adult can be defined by purely behavioral criteria. We must remember that the EEG derives its value because of its correlation with behavioral measures of sleep. If animals are responsive and locomoting, we say they are awake, even if their EEG is high in voltage, a condition that can be created by certain brain lesions and by administration of the muscarinic receptor blocker atropine. [27]

There are a few ambiguous cases in which behavior alone is not sufficient to indicate waking. For example, slow swimming in circles in dolphins occurs during a state of raised arousal thresholds and unilateral EEG synchrony, indicating that it is in fact a sleep state, at least for one half of the brain. [32, 33] Some birds are known to fly continuously for a period of days. [3] Must they be awake throughout these periods? We know that sleep deprived and pathologically sleepy humans engage in automatic behaviors during which the EEG is synchronized and they are unresponsive to the environment. [16] Other "parasomnias" include the locomotion during sleep walking and the vocalizations during sleep talking. Despite their behavioral resemblance to waking, response and arousal thresholds are elevated at these times, precisely the reason these behaviors can be so dangerous. To qualify as sleep, any state must have a raised arousal threshold relative to unambiguous waking. Otherwise we are seeing a state of relaxed wakefulness. In humans we can also add the requirement of lack of awareness of the environment during sleep. However this is a more difficult criterion to use in animals. Even in humans, reduced awareness of certain aspects of the environment can occur while we are focused on others, without meeting any common sense definition of sleep.

What most readily distinguishes REM or paradoxical sleep from nonREM or quiet sleep is the motor activity, first observed in the extra-ocular muscles, which occurs during REM sleep. It is triggered by activation of brainstem reticulo-motor systems. [40] These systems include the paramedian pontine reticular formation, which controls eye movements, as well as the descending reticulospinal systems that cause the distal muscle twitches that characterize REM sleep. The phasic motor activation of REM sleep is usually accompanied by a simultaneous tonic inhibition of muscle tone, resulting in only occasional breakthroughs of limb movement, but frequent eye movements, irregularities in the activity of the respiratory musculature and signs of autonomic motor activation.

I propose the following working definition of REM sleep: **REM sleep is a sleep state in which there is repetitive phasic activation of brainstem reticulo-motor systems.** The simultaneous activation of excitatory and inhibitory motor systems makes it necessary to conduct careful monitoring of motor output and perhaps the monitoring of central motor systems before concluding that no motor activation is occurring. Conversely, the presence of local motor reflexes, such as eye blinks triggered by corneal irritation, would not be sufficient for identification of REM sleep. It would be necessary to provide other evidence of brainstem motor system activation. This definition would classify "active sleep," the term some have used in newborn animals as REM sleep. To fully understand the nature of sleep in any animal, the nature of state specific neuronal activity must be known. To the extent that the neuronal activity patterns may vary across species, there may be corresponding variation in the functional role of sleep.

As will be described below, there are tremendous variations in the amount of sleep exhibited by different species. We must consider the possibility that equally dramatic differences in the pattern of activity of key neuronal cell groups accompany sleep and in particular REM sleep in different species. It is reasonable to hypothesize that the aminergic, GABAergic and glutamatergic cell populations, so important in REM sleep in the cat, have the same pattern of discharge in all animals having REM sleep. This could be true even if the magnitude of activity change may differ. Similarly, one would expect that these same general patterns would hold across development and senescence. However, one can imagine that some species may have evolved qualitatively different aspects of REM sleep. It is not inconceivable that certain species may have "REM sleep" with only one of the monoaminergic cell groups turning off, say the locus coeruleus, while the serotonergic cell group remains active. If this were the case, would it be proper to call the resulting state REM sleep or should a new name be coined for such a sleep state? This is more a semantic issue than a scientific one. Our goal should be to fully characterize the neuronal activity that underlies behavioral states and determine the similarities and differences in this activity across species.

REM SLEEP IN MAMMALS

Zepelin [51] and Zepelin and Rechtschaffen [52] compiled the work that had been done on sleep time in mammals. Some of this work was based

on EEG, EMG and EOG recordings with implanted electrodes in laboratory animals. However, most species were observed in zoos, using behavioral criteria to distinguish sleep from waking and REM sleep from quiet (nonREM sleep). Zepelin's tabulation of the range of sleep times in various placental and marsupial mammal species showed that REM sleep could vary from as little as 40 minutes a day (e.g. in cattle), to as much as 6 hours/day in the black footed ferret [25] and 7 hours/day in the thick tailed oppossum. [52] Zepelin [51] sought some behavioral, ecological, or physiological correlate of this variation. One point that is obvious from the data that he compiled, is that closely related animals do not have similar sleep parameters. Within the rodents, total sleep times range from 7.0-16.6 h and REM sleep times from .8 to 3.4h. Within primates, sleep times range from 8 to 17h and REM sleep times from .7 to 1.9h. Thus the adaptations linked to mammalian order appear to have relatively little to do with determining REM sleep time. For example, primates, with their high intelligence, manual dexterity, bipedal locomotion, long lifespan and other features do not as a group have higher amounts of REM sleep than rodents. Within orders there is a tremendous variation of REM sleep time, even though the amount is relatively fixed for each species.

Zepelin [51] concluded that small animals spend more hours a day asleep. Thus, large animals such as the elephant and giraffe sleep 3.3-3.9 and 4.6 hours, [47] respectively, while the ground squirrel and little brown bat sleep 16.6 and 19.9 hrs. Zepelin also found a small positive correlation between REM sleep and total sleep time. Animals that are small tend to have larger amounts of REM sleep. However, this relationship did not account for much of the variation in REM sleep distribution. Prior developmental studies by Jouvet-Mounier had pointed out that "altricial" animals (those that were born too immature to care for themselves, such as the cat, human and rat) had much larger amounts of REM sleep at birth than "precocial" mammals (animals that are relatively independent soon after birth such as the guinea pig and horse). REM sleep amounts decrease with age in altricial mammals and to a lesser extent in precocial mammals. However, altricial mammals continue to have much larger amounts of REM sleep than precocial mammals as adults. Zepelin showed that immaturity at birth is the single best predictor of REM sleep time throughout life. Before considering the meaning of this relation, we must examine its generality.

SLEEP IN THE ECHIDNA

Of the more than 4,000 existing mammalian species all but three are classified as placental or marsupials. The marsupials are in general more altricial than placentals and many have very large amounts of REM sleep. The third major branch of the mammalian tree is the monotremes. The monotremes are the only mammals that hatch from eggs. The three species are the short and long nosed echidna and the platypus. The long nosed echidna, native to New Guinea is considered endangered and its sleep has not been studied. The short nosed echidna is common in Australia. It eats ants and has a relatively long lifespan (up to 30 years).

If immaturity at birth is correlated with REM sleep time across the entire mammalian line, monotremes should have large amounts of it. After hatching, the hairless and defenseless echidna and platypus newborns climb in the mother's pouch, getting all their nutrition from their mother for a period of 4 to 6 months.

The first study of echidna sleep produced a surprising result. Allison et al., [2] concluded that the echidna had no REM sleep. They found that the echidna exhibited a high voltage EEG during sleep. No periods of sleep with the low voltage EEG and elevated arousal thresholds typical of REM sleep were seen. They saw no rapid eye movements or evidence of phasic motor activation during sleep. Since the echidna was the only monotreme to have had its sleep studied and the only mammal to be shown to lack REM sleep, Allison et al., hypothesized that all the monotremes lack REM sleep.

The monotremes diverged from the other mammalian lines early in the evolution of mammals. Therefore, Allison's hypothesis implies that REM sleep first evolved after the divergence of the placentals and marsupials from the monotremes. Allison concluded that the evolution of REM sleep was linked to the development of vivaparity (live birth). This hypothesis has had an enormous effect on subsequent theories of REM sleep evolution and function. It implied that quiet sleep was the original form of sleep and that REM sleep was a relatively advanced physiological trait. It was consistent with scattered but unconvincing data suggesting a role for REM sleep in learning. It also implied that the reptilian ancestors of mammals did not have REM sleep, since their earliest offspring (the monotremes) did not have this state.

We hypothesized that brainstem neuronal activity during echidna sleep might show aspects of REM sleep even though the forebrain EEG had not shown any low voltage activity during sleep in Allison et al.'s study. We implanted microwire recording electrodes in the midbrain and pons of the echidna, recording neuronal activity throughout the sleep cycle. In the cat, dog and other laboratory mammals, unit activity in most of the units in the brainstem reticular formation is slow and regular during nonREM sleep. During REM sleep, unit activity becomes highly irregular, with periodic burst discharge. This burst discharge spreads to premotor neurons in the extraocular and spinal motor systems, producing the twitching and rapid eye movements that characterize REM sleep. When we recorded reticular neurons in the echidna during periods of high voltage EEG activity, we did not see the nonREM sleep pattern. Figure one shows a typical example of what we saw instead. Unit discharge tended to be irregular and bursty, even though the EEG showed the pattern of nonREM sleep. Figure 2 presents instantaneous rate plots that allow one to compare the discharge pattern of reticular units recorded in the cat, dog and echidna.

We quantified the amount of discharge occurring in bursts in brainstem units in the echidna and compared this data to data we collected in the same anatomical regions in the cat and dog. We found that the irregularity of discharge in the echidna was significantly greater than that seen in nonREM sleep in the cat and dog, but significantly less than that seen in REM sleep. In other words, from the standpoint of brainstem unit activity, the sleep state in the echidna appeared intermediate between REM and nonREM sleep. The echidna did not simply have a quiet sleep state as seen in the cat, dog and rat.

SLEEP IN THE PLATYPUS

We next turned our attention to the platypus. [41] Because the platypus is a semi-aquatic mammal and cannot be confined without severe stress, it has been difficult to capture, maintain and study in captivity. We dealt with these problems by utilizing an electrically shielded, artificial platypus enclosure, implanting telemetry devices to continuously monitor the platypus electroencephalogram (EEG), electrooculogram (EOG), electrocardiogram (ECG) and electromyogram (EMG) while it was active and inactive, in the burrow and underwater. [41]

When the platypus was underwater and quiet, showing its typical diving response, EEG voltage was at its lowest level. A comparable low voltage EEG was also present when the animal was awake in the burrow. At sleep onset, EEG amplitude increased, a state we termed Quiet Sleep with Moderate voltage EEG (QS-M).

Phasic events began as soon as 30 to 90 sec after the onset of QS-M periods. REM sleep, as defined by muscle atonia, phasic EMG potentials and rapid eye movements, was always accompanied by an EEG which was of moderate (REM-M) or high amplitude (REM-H), with consistently

more power in all of the frequency bands assessed than during waking states. In this respect, platypus REM sleep EEG is unlike the low voltage REM sleep EEG seen in adult placental and marsupial mammals. We obtained confirmation of the periods of REM sleep by video recording of posture and behavior in the burrow. We found that all of the REM episodes occurred while the animal was immobile in a curled or prone sleep posture. We found that the phasic EOG and EMG potentials were correlated with rapid movements of the eyes, neck and bill.

The platypus spends 60.1% of its sleep time (> 8 h/day) in a state with the EOG, EMG, ECG and arousal threshold changes typical of REM sleep. This amount is greater than has been seen in any other animal.

HOW DO THE ECHIDNA AND PLATYPUS DATA FIT TOGETHER?

There are both similarities and differences in our findings in the echidna and platypus. Both species have a relatively high voltage EEG throughout sleep. Even during periods of phasic motor activity, the EEG of platypus did not show the low voltage pattern seen during REM sleep in most adult mammals. However, infant placental mammals show a similar pattern of high voltage EEG during active sleep, suggesting that in this respect ontogeny is recapitulating phylogeny.

The phasic motor activation seen in the extraocular, bill and head musculature of the platypus indicates that burst discharge is occurring in its motor and premotor brainstem reticular systems. We saw that the echidna spends a large proportion of its sleep time with a burst-pause discharge pattern in brainstem reticulo-motor systems. Thus, this aspect of REM sleep neuronal activity is present to some extent in the echidna. However, we did not see twitches in neck or eye muscles in the echidna.

Another, perhaps related, difference in the sleep behavior of the echidna and platypus is in the arousal threshold. The platypus is extremely difficult to arouse from sleep and can even be picked up without awakening it. This deep sleep is consistent with its very safe sleep condition, in a burrow that few predators have been able to gain access to. [6] The echidna, in contrast has a relatively unsafe sleeping situation, often out in the open. [15] It has frequently been preyed upon by other animals. It has a relatively low arousal threshold during sleep. When disturbed, it immediately begins digging to attain a safer sleeping or hiding position. Because of its vulnerable sleeping position, any twitching of its large quills would attract attention and endanger it. Thus, the uninhibited twitching shown by the platypus would be maladaptive in the echidna. The mechanism underlying the subdued twitching in the echidna can be seen in its brainstem unit activity. Whereas we see phasic burst discharge in the echidna, the intensity of the bursts is significantly reduced relative to that in the cat and dog. We also found that the bursts during sleep were not generally crosscorrelated in the reticular units of the echidna, while they were in the cat (Fig. 3). Less synchronized burst discharge can explain the lack of twitching seen during sleep in the echidna.

The echidna is thought to have evolved from a platypus-like ancestor. But the divergence occurred over 50 million years ago, an enormous amount of time allowing for a large amount of evolution in sleep behavior, even in the relatively static monotreme line. The question is whether the phasic motor activity of the platypus or the muted brainstem "burstiness" of the echidna is the more recent development. I favor the theory that the platypus pattern represents the more primitive pattern. The behavioral aspects of REM sleep in the platypus are similar to those in placental and marsupial mammals and particularly to the vigorous phasic activity seen in neonates. The lack of EEG voltage reduction in REM sleep in the platypus is similar to the neonatal pattern in other mammals. [13, 29] The large amounts of REM sleep also fit the neonatal pattern. [51] So the sleep of the platypus fits well with the general mammalian pattern, at least that of neonates. The echidna's lack of prominent motor activation during sleep is unique. The most parsimonious conclusion is that the echidna's sleep pattern is the more recently evolved. The absence of other mammalian species without phasic motor activity during sleep suggests that the evolutionary route that allowed the echidna to reduce its brainstem activation during sleep may not have been open to other species. Once REM sleep evolved into a state that recruited neurons in the forebrain, in addition to the brainstem, a reduction in burst discharge and a reversal of forebrain changes may not have been possible.

The common element of sleep in both examined monotreme species is high voltage EEG during phasic activation of brainstem reticulo-motor systems. This combined with the presence of a relatively high voltage EEG in neonates suggests that the EEG voltage reduction seen in adult mammals during REM sleep is a more recently evolved feature of REM sleep. If dreaming requires such forebrain EEG "activation" one may speculate that dreaming evolved after the divergence of the monotreme line from the marsupials and placentals. Of course it has been argued that even in humans, dreaming is unrelated to EEG state and is not restricted to REM sleep. [38]

REPTILIAN SLEEP

We find a REM sleep state in the platypus and aspects of REM sleep in the echidna. All other examined mammals have been found to have REM sleep [reports that the dolphin lacks REM sleep [32] are inconsistent with earlier work [8, 9] and with more recent work. [34]] REM sleep is known to be present in birds. These findings suggest that reptiles, the common ancestors of birds and mammals may have REM sleep. If REM sleep is not present in reptiles it must have evolved twice. Even if it evolved twice, one would expect some precursor state to have existed in reptiles ancestral to both mammals and birds, given the (apparently) similar form of REM sleep in birds and mammals.

The three major orders of living reptiles are 1. The lizards and snakes, 2. The crocodilians and 3. The chelonians (turtles and tortoises).

Tauber et al., [44] reported evidence for REM sleep in the chameleon lizard. They reasoned that this animal, having very mobile active eyes in waking would be more likely to show eye movement periods during sleep. They, like most subsequent researchers working with reptiles, found relatively little modulation of forebrain EEG across the sleep-wake cycle, compared to the dramatic modulation in mammals. Some spiking occurred in forebrain leads during sleep, but no change in EEG occurred during periods of rapid eye movement. In "REM" sleep, one eye could be open while the other remained shut. No change in muscle tone occurred during sleep. No arousal threshold testing is described in this brief report.

Tauber et al., [45] report on sleep in the lizard *Ctenosaura pectina*. They report an increase in EEG voltage with arousal, accompanied by an increase in spikes recorded from the cortex. This contrasts to the blocking of spikes with arousal that they reported in the chameleon. The EEG voltage increase with arousal was seen in brainstem as well as forebrain leads. During sleep, EEG amplitude was reduced. Arousal threshold was reported to be elevated. Two to three hours after sleep onset, eye movements began to appear independently in the two eyes. These eye movement periods recurred at 4-25 minute intervals throughout the sleep period. The duration of these periods is not described. Heart rate slowed during eye movement periods. Tauber et al., report an elevation of arousal threshold throughout sleep, but do not report it separately for rapid eye movement periods or quantify arousal threshold with sleep.

Ayala-Guerrero and Huitron-Resendiz [5] conducted a similar investigation of this same species and also concluded that *Ctenosaura pectinata* had REM sleep, although the example they show looks very much like waking. However, Flanigan et al., [7] investigated this same species and also *Iguana iguana*. They saw no evidence for REM sleep in either species.

Huntley [21] reported that the desert iguana *Dipososaurus dorsalis* has REM sleep. This state was identified largely on the basis of EEG and EMG measures. Huntley found that a high voltage EEG accompanied waking in the iguana. A low voltage EEG pattern characterized quiescent behavioral sleep pattern. "Paradoxical sleep" periods were characterized by a return to the waking high voltage while the EMG reached minimal levels. In contrast to the high and irregular respiratory rate of waking, the paradoxical sleep state had a cessation of respiration. Heart rate was much slower than heart rate during waking and was variable as in waking. Paradoxical sleep time was greater at higher temperatures. Arousal thresholds for paradoxical and quiet sleep states were not analyzed. The percentage of times a standard shock delivered to thoracic leads aroused the animals was determined. It was found that sleep was accompanied by a reduced response percentage. Unfortunately, relatively few tests using this method were performed during "paradoxical sleep," so there is uncertainly as to whether the reduction in response frequency in this state was real. The absence of threshold tests (using ascending stimulation intensities) also makes it uncertain if the states scored as paradoxical were in fact sleep, as opposed to waking states. Huntley does not provide any evidence of phasic motor activity during this state.

A series of papers in the crocodilian *Caiman sclerops* concludes that this reptile does not have REM sleep. Flanigan et al., [12] found that caimans had small changes in the EEG across the sleep wake continuum. Forebrain EEG spikes increased with behavioral quiescence and decreased with arousal. Sleep deprivation increased spiking during recovery sleep. These workers saw no evidence of paradoxical sleep. This same species was studies by Warner and Huggins [48] and Meglasson and Huggins. [30] They did not see the frequent spiking noted by Flanigan et al. They attribute this difference to the submersion of the nares of the animals in the Flanigan et al., study. They felt that the difference was related to cessation of respiration or to nasal stimulation. Also in contrast to the Flanigan study, they report slow waves during quiescent in their animals. They suggest that the state with slow waves was not seen in the prior study. Flanigan et al., had reported that more than one week of adaptation was required before animals showed sleep. Warner and Huggins saw sleep within hours of introduction into their recording situation. Warner and Huggins did not see evidence of REM sleep, but they point out that, because they did not record for 24-hour periods, they could easily have missed it. They attribute many of the differences in their findings and the findings of Flanigan et al., to the presence of other caimans in their recording situation, relaxing the recorded animal, or to the use of higher temperatures and younger animals in their study.

Flanigan et al [10] also investigated two species of Chelonians (turtles and tortoises). They report no evidence for REM sleep in either species.

These data leave the question of the existence of REM sleep in reptiles unresolved. Several problems outlined above may explain "false positive" reports of REM sleep in reptiles. In particular, transient arousals might masquerade as REM sleep. Waking can only be distinguished from REM sleep through the use of arousal threshold tests.

On the other hand it is certainly possible that "false negative" reports have overlooked periods of REM sleep in reptiles. Brief "bird-like" periods of REM sleep might easily be missed. Without behavioral observation, REM sleep periods might be mistaken for waking. It is also possible that some reptiles such as *Dipsosaurus dorsalis* have REM sleep while others such as *Caiman sclerops* do not. However the ubiquity of REM sleep in mammals makes the search for an underlying commonality of REM and nonREM sleep states in reptiles attractive. One does not want to uncritically accept the principle that certain reptiles have REM sleep with aspects of autonomic and muscle tone control identical to mammals and that others completely lack this state, without first looking for replication of the key positive and negative findings.

A more fundamental issue is one of state definition. Since neocortex is absent in reptiles, there is no particular reason to expect a mammalian REM sleep-like voltage reduction. Indeed the Huntley paper reports just the reverse pattern; increased EEG amplitude in REM sleep and waking. However, no other reptilian study, even those purporting to see REM sleep report such a pattern. Cardiac variability while correlated with REM sleep in most mammals does not always differentiate REM sleep from waking. In the mole, heart rate is significantly less variable in REM sleep than in nonREM sleep. [1]

In keeping with the discussion at the beginning of this chapter, we propose that this uncertainly about the identification of REM sleep in reptiles can only be resolved by monitoring neuronal activity along with arousal thresholds. In particular, the activity of brainstem cholinergic, serotonergic and noradrenergic cell groups must be sampled to better characterize the neuronal activity correlates of the observed macropotentials (EEG, ECG, EOG, EMG) characteristic of each state. Once these activity correlates are known, we will understand which if any elements of brainstem neuronal activity are correlated with the defined state. This will permit a more meaningful characterization of state. It will also allow a powerful insight into the evolution of sleep cycle discharge patterns in aminergic and cholinergic cell groups. Because these groups are centrally involved in human psychopathology as well as state control, understanding how their state related activity evolved could be of great clinical significance. In particular it could lead to the identification of receptor and other rate control mechanisms that may differ in reptiles, mammals and birds.

CONCLUSIONS

We have found that the platypus has a sleep state with eye movements and twitching of the head and bill. The echidna has not been observed to have such phasic motor activity during sleep. However the echidna does have a pattern of regular burst discharge in brainstem reticular cells similar to, but less intense than that seen in REM sleep. Both monotreme species have these periods of "brainstem activation" during periods of EEG synchronization. These findings suggest that EEG voltage reduction during REM sleep is a more recently evolved feature of this state; that REM sleep in mammals originated as a brainstem state.

The presence of REM sleep in all three branches of the mammalian tree suggests that it or a very similar state was present in the earliest mammals. REM sleep is present in birds. The ubiquity of REM sleep in mammals and its presence in birds is most parsimoniously explained if one hypothesizes a single origin of this state in the common reptilian ancestors of birds and mammals. This hypothesis would predict a REM sleep state or at the least a state with many aspects of REM sleep in living reptiles. Studies at the neuronal level are necessary to test this hypothesis.

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Figure captions

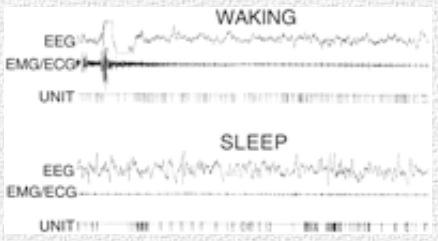

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Fig. 1. Unit discharge of a representative neuron recorded in nucleus reticularis pontis oralis of the echidna during waking and sleep. Note irregularity of neuronal discharge during sleep. EEG (electroencephalogram), EMG/ECG electromyogram/electrocardiogram), Unit, pulse output of window discriminator triggered by neuron. This and subsequent figures reprinted with permission from Siegel et al., 1996.

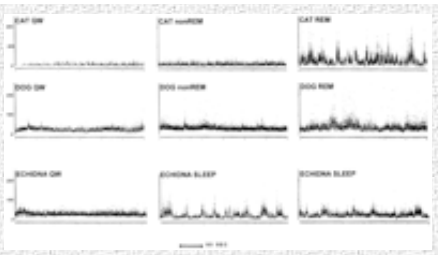

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Fig. 2. Instantaneous compressed rate plots of representative units recorded in nucleus reticularis pontis oralis of cat, dog and echidna. Each point represents the discharge rate for the prior interspike interval. In cat QW and SWS (nonREM sleep) 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.

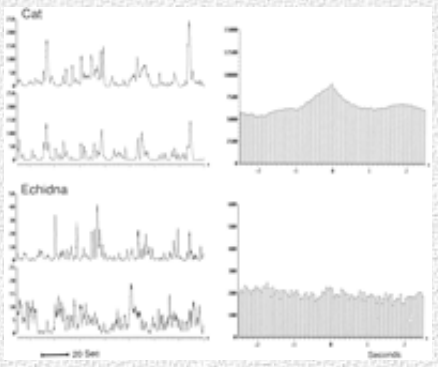

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Fig. 3. Rate histograms and crosscorrelogram of discharge in a pair of cat reticularis pontis oralis units recorded during REM sleep (top), compared with a pair of echidna reticularis pontis oralis units recorded during sleep (bottom). Crosscorrelograms of each pair computed at 50 msec binwidth are shown at right. Unit pairs in both the cat and echidna were recorded from adjacent microwires on a single bundle of 32 m microwires. While most cat and dog units fire synchronously and are crosscorrelated during REM sleep (12), none of the echidna unit pairs were crosscorrelated in sleep.

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