The Royal Society

Monotremes and the evolution of rapid eye movement sleep

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Early studies of the echidna led to the conclusion that this monotreme did not have rapid eye movement (REM) sleep. Because the monotremes had diverged from the placental and marsupial lines very early in mammalian evolution, this finding was used to support the hypothesis that REM sleep evolved after the start of the mammalian line. The current paper summarizes our recent work on sleep in the echidna and platypus and leads to a very different interpretation. By using neuronal recording from mesopontine regions in the echidna, we found that despite the presence of a high-voltage cortical electroencephalogram (EEG), brainstem units fire in irregular bursts intermediate in intensity between the regular non-REM sleep pattern and the highly irregular REM sleep pattern seen in placentals. Thus the echidna displays brainstem activation during sleep with high-voltage cortical EEG. This work encouraged us to do the first study of sleep, to our knowledge, in the platypus. In the platypus we saw sleep with vigorous rapid eye, bill and head twitching, identical in behaviour to that which defines REM sleep in placental mammals. Recording of the EEG in the platypus during natural sleep and waking states revealed that it had moderate and high-voltage cortical EEGs during this REM sleep state. The platypus not only has REM sleep, but it had more of it than any other animal. The lack of EEG voltage reduction during REM sleep in the platypus, and during the REM sleep-like state of the echidna, has some similarity to the sleep seen in neonatal sleep in placentals. The very high amounts of REM sleep seen in the platypus also fit with the increased REM sleep duration seen in altricial mammals.

Our findings suggest that REM sleep originated earlier in mammalian evolution than had previously been thought and is consistent with the hypothesis that REM sleep, or a precursor state with aspects of REM sleep, may have had its origin in reptilian species.

Keywords: sleep; mammals; brainstem; reptile

1. A REVIEW OF SLEEP PHYSIOLOGY IN MAMMALS

Sleep in mammals can be divided into two distinct stages: rapid eye movement (REM) and non-REM. Non-REM sleep typically occurs at sleep onset. In this state, muscle tone and movement decrease, respiration becomes regular and the voltage of the cortical electroencephalogram (EEG) increases.

Non-REM sleep is followed by REM sleep (also called paradoxical sleep, dream sleep, desynchronized sleep and active sleep). REM sleep takes its name from the rapid eye movements that occur during this state. In humans, dreams are frequently reported in this state (Aserinsky & Kleitman 1953). The cortical EEG in REM sleep is low voltage, virtually indistinguishable from the EEG of waking. Hippocampal theta is present in REM sleep as it is in active waking. Brain metabolic activity is extremely high, often exceeding levels seen in waking. At the same time, homeostatic control of respiration and thermoregulation are reduced. Respiration becomes irregular during REM sleep and it does not respond as rapidly to CO_2 challenges as it does in non-REM sleep (Siegel 1994; Rechtschaffen & Siegel 1999). The body's temperature tends to drift towards ambient temperature, as if thermoregulation is suspended, a return to the reptilian pattern. Penile erections occur, although often with no relation to dream content.

The differences in the phenomenology of REM sleep and non-REM sleep have been examined at the neuronal level. In non-REM sleep, neuronal activity is greatly reduced in the brainstem (Siegel 1994). In the cortex and thalamus, rate does not decrease much from waking values, but the pattern changes (Rechtschaffen & Siegel 1999). Neurons tend to fire rhythmically and in synchrony with neighbouring neurons. The nucleus reticularis of the thalamus is the key structure coordinating this synchrony (Steriade *et al*. 1993). This rhythmic discharge of thalamus and cortex prevents the accurate transmission of sensory signals, protecting sleep from external disturbance and preventing accurate perception of the environment. Despite the rhythmic discharge of cortical neurons, overall metabolism is greatly reduced in the cortex and throughout the brain in non-REM sleep.

Despite our common experience that sleep follows reduction of sensory input, such reduction is not sufficient to generate sleep. Rather, non-REM sleep is actively induced by populations of neurons that are selectively active in this state. One particularly important group of such neurons is located in the preoptic region of the basal

forebrain. Stimulation of these neurons (which are activated by heat) induces sleep. Lesion of this region produces insomnia. These neurons project to hypothalamic and brainstem neurons, which in turn control the thalamic mechanisms that synchronize neuronal populations throughout the brain (McGinty & Szymusiak 1990).

In REM sleep, a very different pattern of neuronal activity occurs. In the brainstem and neocortex, neurons fire in rapid bursts. Activity often exceeds that seen in very active waking. The discharge pattern resembles that of waking, not the regular slow discharge pattern seen in non-REM sleep (Siegel 1994). However, despite the waking-like activity of the brain, sensory inputs are not processed and awareness of the environment is absent. There is some evidence that sensory inputs are actively blocked at the periphery during REM sleep (Pompeiano 1970). The complete absence of consciousness, despite the presence of cortical and brainstem activation, cannot be easily explained by the phasic inhibition of sensory input and remains a mystery. During REM sleep, muscle tone in most skeletal muscles is abolished. This is thought to be a protective mechanism preventing the intense brainstem activation from producing movement that would injure the sleeper. The reduction in muscle tone is due, at least in part, to active inhibition of motoneurons (Chase & Morales 1990).

REM sleep is generated by the brainstem. If one separates the brainstem from the forebrain by transecting the neuraxis at the midbrain, REM sleep remains present below the level of the transection and absent in front of the transection. The key neuronal groups responsible for REM sleep generation are located in the pons. The pontine reticular formation has groups of cells that are selectively active in REM sleep ('REM sleep-on cells') and groups of cells that are selectively inactive in REM sleep ('REM sleep-off cells') (Siegel 1994). The noradrenergic cells of the locus coeruleus and the serotonergic cells of the raphe nucleus are all REM sleep-off. The REM sleep-on population is heterogeneous. Current evidence indicates that some REM-on cells are cholinergic, some are GABAergic (Nitz & Siegel 1997*a*,*b*), and some glutamatergic (Lai & Siegel 1991; Sakai & Koyama 1996). It is likely that peptides and other neurotransmitters are also involved. Most cells in the brainstem reticular formation fire in bursts in conjunction with movements in waking and also fire in bursts during REM sleep. These are pre-motor cells that generate the twitching that characterizes REM sleep (Siegel & McGinty 1977). Together, the REM-waking active cells, the REM-on cells and the REM-off cells generate the major phenomena of REM sleep.

2. EVIDENCE BEARING ON THE FUNCTION OF SLEEP

We do not know what biological need generates non-REM sleep and what feedback mechanism terminates it. The same is true for REM sleep. It is often supposed that because of their very different patterns of brain activity, REM and non-REM sleep serve very different functions. However, there is no persuasive evidence for this. It is known that under certain conditions the brain seems to accumulate distinct 'debts' for REM and non-REM sleep. REM sleep deprivation will produce a rebound in REM sleep at the expense of non-REM sleep and vice versa (Rechtschaffen & Siegel 1997).

Although we do not know the function of sleep, it is clearly essential. Complete sleep deprivation in rats produces death faster than complete food deprivation (Rechtschaffen *et al*. 1989). Deprivation of just REM sleep or just the deep stages of non-REM sleep is also lethal, but the process takes longer (Kushida *et al*. 1989; Rechtschaffen & Siegel 1999). The cause of death is unclear at the moment, although thermoregulatory problems appear to be involved.

Some clues to the function of sleep emerge from its developmental time-course. REM sleep as a proportion of sleep time is greatest in young mammals. A human baby may have 7 h of REM sleep at birth, but this decreases to 1.5 h by adulthood (Roffwarg *et al*. 1966). Mammals that are born relatively immature have more REM sleep not only at birth, but even in adulthood, when compared with animals that are 'precocial'. For example humans, cats and rats, all born immature ('altricial') have more REM sleep as adults than guinea pigs, horses and giraffes, which are born relatively mature (Zepelin 1994).

Some conclusions are apparent. Because of the association of dreaming with REM sleep and the rich symbolic content of dreams, it has often been speculated that this state has some unique role in higher cerebral functions, symbolic thought and learning. Although we cannot exclude this possibility in humans, clearly the phylogenetic data do not support this conclusion. Humans and primates are not unique in their amounts of REM sleep. Cats, opossums, armadillos and other mammals not known for their intellectual achievements have far more REM sleep, whether calculated in hours per day or as a percentage of total sleep time, than humans. Why do they have so much REM sleep? Can the phylogenetic approach help identify the neurological or behavioural capabilities that are linked to the emergence of this state? At the most basic level, can the phylogenetic data tell us whether REM sleep is a relatively old state or whether it is a new invention of the mammalian line?

3. PHYLOGENETIC STUDIES OF SLEEP IN REPTILES, BIRDS AND MONOTREMES

We undertook our studies of the monotremes to address the question of when REM sleep evolved. Before our studies, some had concluded that REM sleep had evolved relatively recently. This conclusion was supported by certain studies of reptiles and one pivotal study of the monotreme echidna.

The study done by Allison *et al*. (1972) of sleep in the echidna found that this animal had none of the EEG or eye movement markers of REM sleep. Rather, echidnas had long periods of what appear to be non-REM sleep. These findings led Allison *et al*. (1972) to conclude that REM sleep had evolved after the divergence of the monotreme line from the placental and marsupial lines.

Supporting this conclusion were a number of subsequent studies in reptiles, which reported states of quiescence that resembled the state of non-REM sleep seen in mammals. Respiration was regular. Spiking was seen in basal ganglia regions. This spiking resembled that seen in the

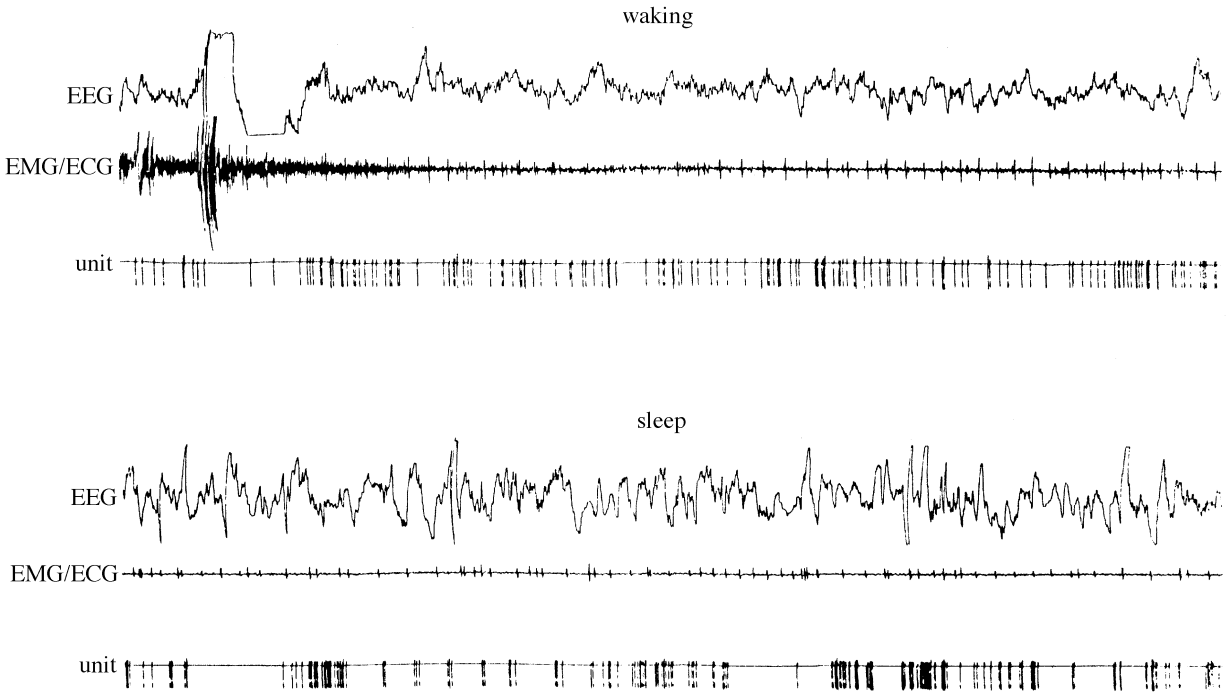

Figure 1. Sleep in the echidna. Sleep with high-voltage cortical EEG is accompanied by phasic unit discharge in the echidna. EEG, sensorimotor electroencephalogram; EMG/ECG, nuchal electromyogram with electrocardiogram pickup. Duration of samples is 30 s. Reprinted from Siegel *et al.* (1996), with permission.

amygdala during non-REM sleep in mammals. No periods of phasic motor or eye movement activity were seen that were reminiscent of REM sleep (Flanigan 1973; Flanigan *et al.* 1974; Meglasson & Huggins 1979). These findings led to the conclusion that reptiles did not have REM sleep. If this was the case across the entire reptilian line, it would appear likely that REM sleep evolved in mammals, linked presumably to some aspect of mammalian physiology or behaviour.

Other evidence does not support the conclusion that REM sleep evolved after the separation of monotremes from placentals and marsupials. Although methodologies differ, some examinations of reptilian sleep had produced evidence for phasic events and even eye movements during sleep (Peyrethon & Dusan-Peyrethon 1968; Huntley 1987; Ayala-Guerrero 1991). If this indicates the presence of REM sleep and if Allison *et al.*'s (1972), conclusion is correct, it would suggest that REM sleep evolved before the mammalian line and that perhaps the echidna has lost REM sleep.

Another major clue to the evolutionary history of REM sleep is the nature of sleep in birds. Some birds have periods of suppression of neck muscle tone during sleep (Amlaner & Ball 1994). Eye movements occur during these states, which last only a few seconds. Other birds retain muscle tone during these periods of sleep with rapid eye movements. The presence of REM sleep in birds suggests one of two possibilities. The first is that REM sleep evolved twice, once in birds and once in mammals. The second is that REM sleep evolved in the common reptilian ancestors of both birds and mammals. This would suggest that some or all reptiles would have aspects of REM sleep. The small amounts of REM sleep seen in birds does not fit with the major relationship hypothesized in mammals, between immaturity at birth and high amounts of REM sleep. Even birds that are completely unable to thermoregulate and care for themselves at birth have extremely small amounts of REM sleep compared with comparatively immature mammals (Amlaner & Ball 1994).

A major problem in evaluating the studies in birds and reptiles is the identification of REM sleep from polygraphic measures. EEG is not a reliable indicator of state. In neonates, EEG does not show the reduction in amplitude and relative increase in high frequency activity seen in adults (Emde & Metcalf 1970). Therefore, one should not necessarily expect EEG changes with REM sleep. Whereas muscle tone suppression is a frequent correlate of state, many birds and mammals do not have clear muscle tone suppression during REM sleep (Pivik *et al.* 1981; Amlaner & Ball 1994; Siegel 1994). Eye movements are not present in 'REM' sleep in mammals that do not have many eye movements while awake, such as the mole (Allison & Van Twyver 1970). The presence or absence of eye movements during sleep in monotremes, reptiles and birds does not clearly identify the observed state as REM sleep.

4. STUDIES OF SINGLE-UNIT ACTIVITY DURING SLEEP IN THE MONOTREME ECHIDNA

With these considerations in mind, we sought a more objective way to address the question of identification of sleep state. Whereas the epiphenomena of REM sleep, the changes in EEG, electromyogram (EMG) and eye movement, could not clearly identify state, we felt that examination of neuronal activity could. As outlined above, REM sleep is generated by a population of neurons in the brainstem reticular formation. The phasic

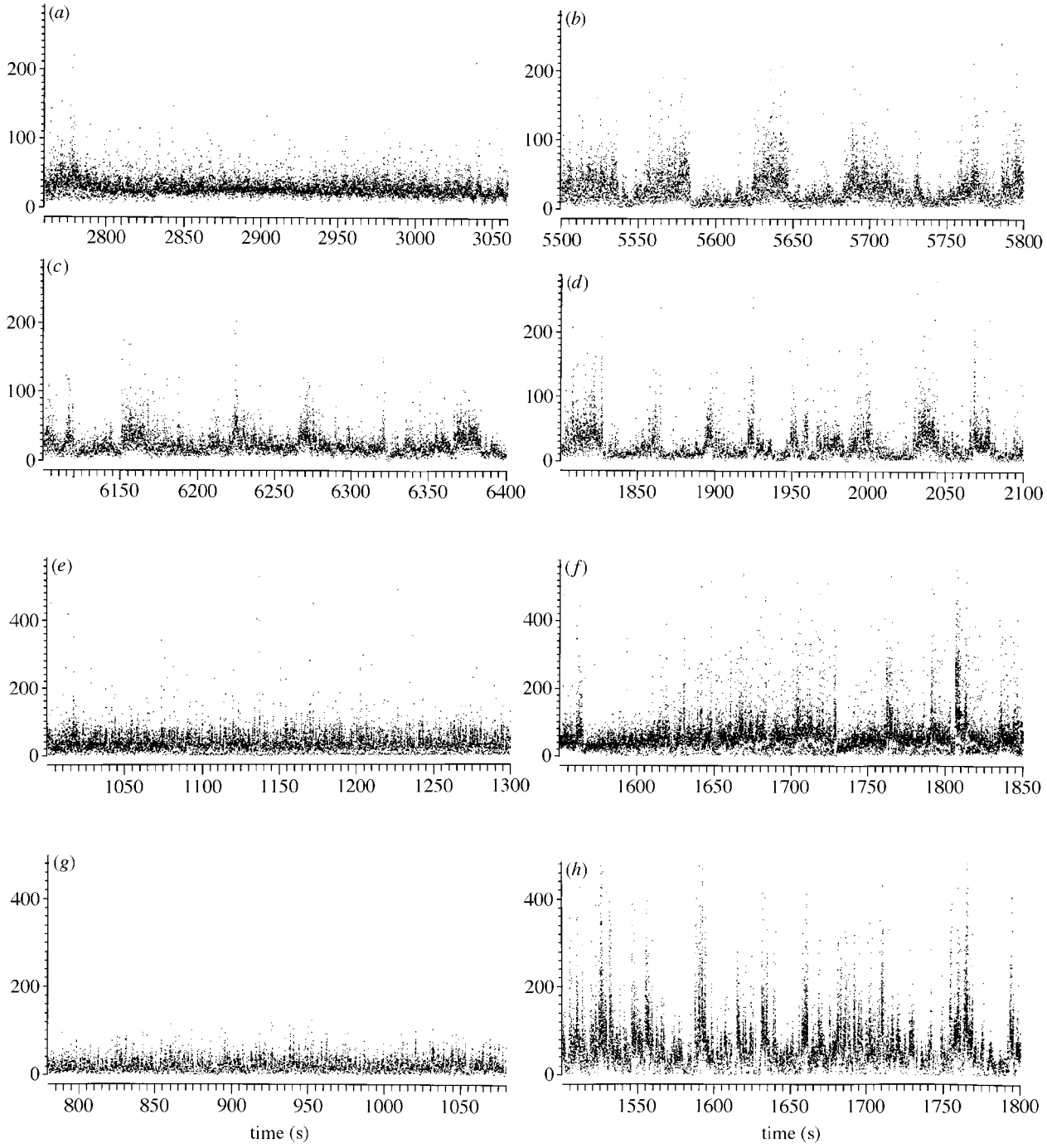

Figure 2. Instantaneous rate plots of representative units recorded in the nucleus reticularis pontis oralis of the echidna (*a*, *b*, *c* and *d*), dog (*e*,*f*) and cat (*g*, *h*). Each point represents the discharge rate for the prior interspike interval. In the echidna, discharge rate is regular during quiet waking (*a*), as in quiet waking in the dog (*e*) and cat (*f*). Discharge in the echidna increases and becomes more variable in sleep, subdivided here into S1 (*b*), S2 (*c*) and S3 (*d*), states with progressively more slow waves in the EEG. This increased rate and variability parallels that seen in REM sleep in the dog (*f*) and cat (*h*). Reprinted from Siegel *et al.* (1996), with permission.

motor activation of REM sleep originates in the discharge pattern of these cells. By examining unit activity across species, one could more directly compare and contrast the nature of neuronal activity that characterizes sleep. Does the brainstem of the echidna, an animal which seems to lack the cortical slow wave indicators of REM sleep, have a unit discharge pattern indicative of REM sleep or of non-REM sleep? This kind of approach appeared to us to be a useful way of re-examining the question of when REM sleep evolved.

The medial reticular REM-waking active cells are the most easily recorded of the cell types that would enable us to characterize sleep state. We reasoned that if an REM sleep-like state existed in the echidna it could be identified by the characteristic burst–pause discharge pattern seen in the majority of medial reticular cells of placental mammals during REM sleep.

We used microwire recording techniques that enabled us to record the activity of these cells while the animal went about its normal waking and sleep behaviours (Siegel *et al.*

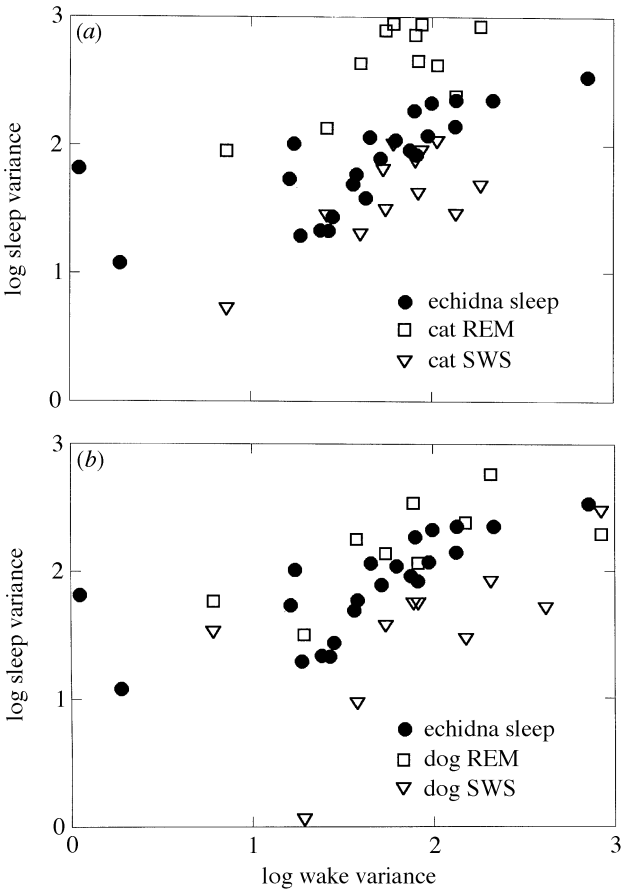

Figure 3. Quiet waking variance plotted against sleep variance in the echidna. Points in the echidna are plotted along with REM sleep and non-REM sleep values as a function of quiet waking in (*a*) the cat and (*b*) the dog. Note that the majority of the points representing echidna units fall between those of cat or dog units recorded in REM sleep and those recorded in non-REM sleep. This illustrates our finding that there is: (i) a significant increase in variance during sleep in the echidna compared with a decrease in variance in non-REM sleep in the cat and dog; and (ii) this variance increase is significantly smaller than that seen in REM sleep in cat and dog reticular units. Reprinted from Siegel *et al*. (1996), with permission.

1996). We also recorded cortical EEG, neck muscle activity and eye movement. Figure 1 shows what we found. In agreement with Allison's previous findings, we saw that the cortical EEG during sleep resembled the non-REM pattern. We did not see any rapid eye movements during behavioural quiescence like the pattern seen in placental REM sleep.

However, the unit discharge pattern did not look like the discharge pattern of medial reticular units seen in non-REM sleep. As figures 1 and 2 show, reticular unit discharge was irregular during sleep, somewhat similar to the pattern seen in REM sleep. To quantify this relationship, we compared cells' sleep discharge rates with their quiet waking discharge rates. In placentals, virtually all pontine medial reticular formation units increase discharge rate variability during REM sleep, with respect to their quiet waking rates. In quiet sleep, variability remains the same or decreases relative to quiet waking discharge rates. The relation between quiet waking and REM and non-REM discharge rate variability is represented in figure 3. The values for the echidna are plotted on the same axes. It can be seen that the variability of discharge increased in medial reticular units during sleep. In other words, unit activity changed in the direction of the placental REM sleep pattern, although to a lesser extent than in our comparison data from cats and dogs.

In placental mammals, neurons not only fire in bursts during REM sleep, but adjacent neurons tend to fire their bursts at the same time. This can be seen in correlations of simultaneously recorded units. Synchronized bursts in adjacent reticulospinal neurons would release glutamate onto motoneurons resulting in phasic excitation sufficient to overcome the tonic motoneurons quiescence during this state and produce observable twitches (Siegel 1979; Chase & Morales 1990). In contrast to the placental pattern, none of the ten pairs of echidna units examined showed a positive cross-correlation (figure 4). This lack of synchronous discharge may account for the lack of prominent twitching during REM sleep in the echidna, in contrast to the pattern in other mammals.

Because REM sleep times are so much greater in young animals that are immature at birth (Jouvet-Mounier *et al*. 1970), it is possible that very young echidnas might show twitching during sleep. One cannot of rule out the possibility that adult echidnas might, under some conditions, show phasic motor activity during sleep. However, both our work and Allison's work suggest that such activity is at least very uncommon in laboratory situations in which other mammals have shown this activity.

Our echidna findings lead us to conclude that the brainstem of the echidna is experiencing a pattern of unit activation like that seen in REM sleep, even while the forebrain generates the non-REM sleep EEG pattern. In short, a state resembling REM sleep is present in the brainstem, while the forebrain remains in a state resembling non-REM sleep.

5. BEHAVIOURAL OBSERVATIONS OF SLEEP IN THE PLATYPUS

Our findings in the echidna encouraged us to do further study in the other monotreme available for study, the platypus. (The third living monotreme species is the long beaked echidna, native to New Guinea. This species is endangered and is not available for study.) The echidna and platypus lines diverged 60–80 million years ago (Ma BP) (Westerman & Edwards 1991). Unlike the highly encephalized echidna, the platypus has a lisencephalic cortex. These differences in neuroanatomy and their long independent evolutionary course could have caused substantial differences in the evolution of sleep in the echidna and platypus. Conversely, any properties of sleep common to both species would most likely have been present in the earliest monotremes and possibly in the common mammalian ancestor.

We found that the platypus is a surprisingly deep sleeper. It was possible to open our artificial platypus enclosure and watch the platypus sleep without awakening it. The platypus could be in any one of a number of postures during sleep (figure 5). In the older platypus literature, we came across a description of a platypus remaining asleep even while its burrow was dug open (Burrrell 1927), consistent with our observations. We saw the platypus show the combination eye, head and neck twitching that

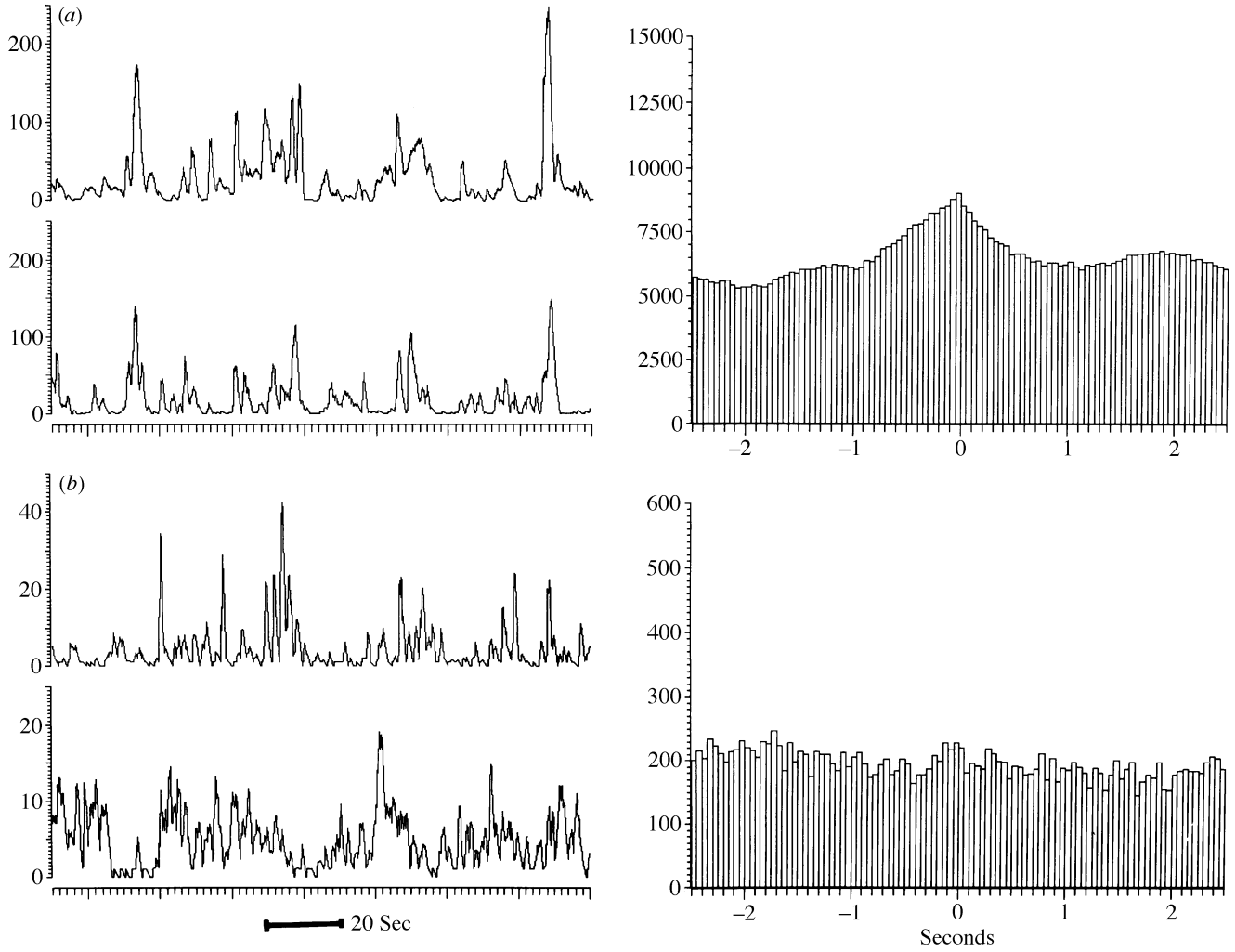

Figure 4. Rate histogram and cross-correlogram of discharge in (*a*) a pair of cat reticularis pontis oralis units recorded during REM sleep, compared with (*b*) a pair of echidna reticularis pontis oralis units recorded during sleep. Counts per second are recorded on the *y*-axes on the left; cross-correlograms of each pair computed at 50 ms binwidth are shown at the right. Unit pairs in both the cat and echidna were recorded from adjacent microwires on a single bundle of 32 µm microwires. Whereas most cat and dog units fire synchronously and are cross-correlated during REM sleep (Siegel *et al.* 1996), none of the echidna unit pairs were cross-correlated in sleep. Reprinted from Siegel *et al.* (1996), with permission.

characterizes REM sleep. These head and eye movements indicate phasic activity in the brainstem. Whereas the absence of one or more of these aspects of REM sleep does not prove the absence of REM sleep, their presence clearly indicates a commonality between platypus REM sleep and that of placental mammals. Bennett (1860), nearly a century before the discovery of REM sleep, reported that very young platypus showed swimming movements of their forepaws while asleep, indicative of dreaming. In our adult platypus, we never saw paw movements during sleep, so perhaps the motor activity becomes restricted to the neck and bill with maturity.

6. POLYGRAPHIC SIGNS OF SLEEP IN THE PLATYPUS

We next sought to determine if the electrical signs of sleep in the platypus were similar to those in other mammals (Siegel *et al.* 1997). Because they are very delicate animals and are aquatic in nature, it would be extremely difficult to record unit activity during natural sleep–waking cycles as we did in the echidna. However, it was possible to record cortical EEGs, neck muscle activity and electrocardiograms (ECGs) during sleep using an implanted telemetry system.

We found that the behaviourally identified REM sleep stage occurred while the EEG was moderate or high in voltage, i.e. as in non-REM sleep. Thus, in this respect, the REM sleep state of the platypus resembled the sleep state seen in the echidna. Both apparently have neuronal activation in the brainstem while the cortex is showing the high-voltage pattern of non-REM sleep.

Like the unit activity in the brainstem, the heart rate is irregular during REM sleep in mammals. At the same time, the heart rate during REM sleep loses the very marked, regular 'sinus arrhythmia', the respiratory related increase in rate during inspiration and decrease during expiration. The platypus shows the REM sleep pattern during sleep with phasic activity, another indication of its similarity with REM sleep.

When we scored the amount of REM sleep in the platypus using an adaptation of the standard sleep scoring rules (Rechtschaffen & Kales 1968), the platypus had more than 8 h d^{-1} of REM sleep, far more than any

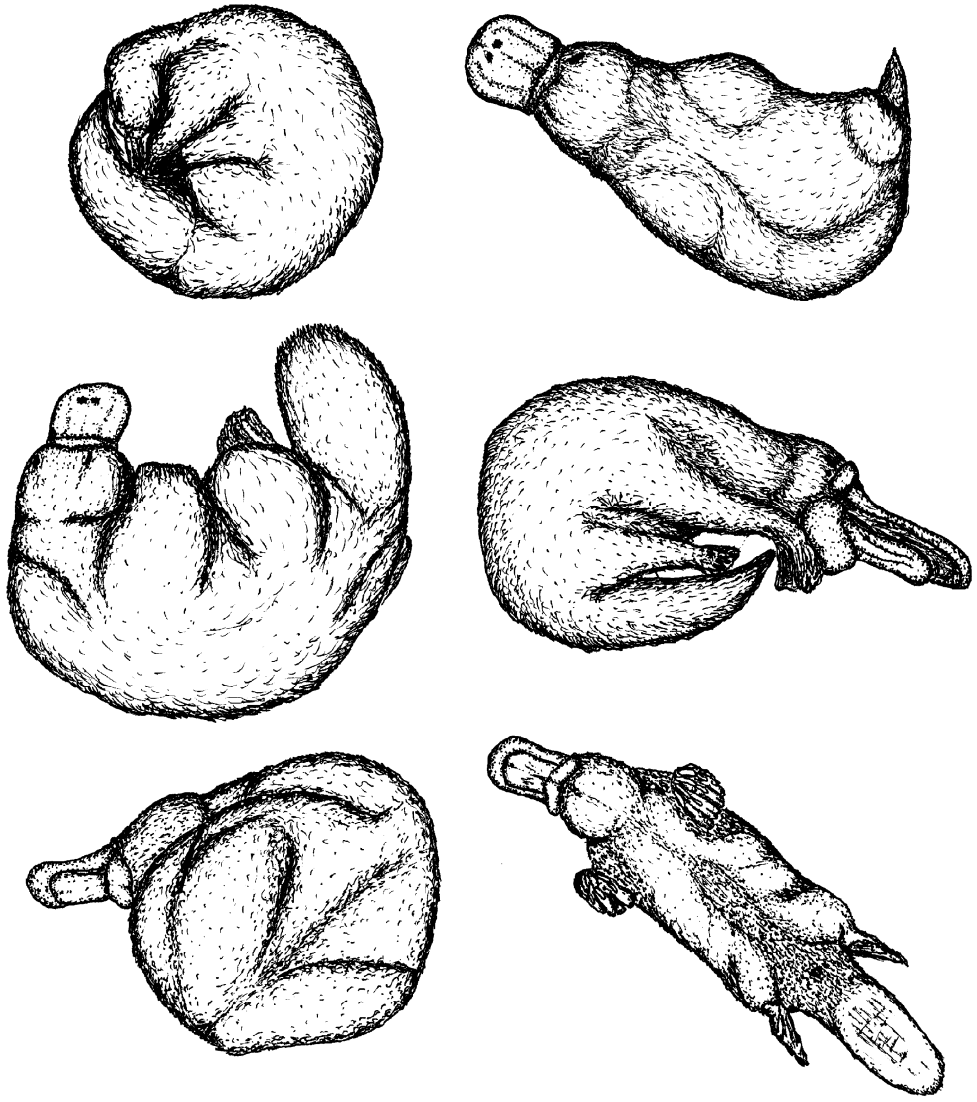

Figure 5. We found the platypus asleep in a number of postures, illustrated here.

other mammal. The nearest 'competitor', the black footed ferret, has less than 6 h d^{-1} (Marks & Shaffery 1996)

7. WHY DOES ECHIDNA REM SLEEP DIFFER FROM THAT IN THE PLATYPUS?

Given that both the platypus and the echidna seem to have aspects of REM sleep, one can ask why echidnas do not have the twitching that characterizes REM sleep in the platypus and many other mammals. We think that this difference may stem from the marked differences in vulnerability between the platypus and the echidna in their natural environments. Because the platypus sleeps safely in a burrow, there is little selective disadvantage in a sleep pattern that produces marked twitching of the body as brainstem neurons burst during REM sleep. Platypus thus have highly visible twitching during REM sleep, more so than that even in carnivores such as the cat and dog. In contrast, the twitching of an echidna's spines would be both audible and visible to a predator in the exposed environment where they sleep. Echidnas would thus have a selective advantage if brainstem neurons had a decreased amount of neighbour-to-neighbour coupling when they entered the bursty firing pattern of REM sleep, as has been observed (Siegel *et al*. 1996), thereby reducing the vigour of each twitch. This speculation is supported by phylogenetic analysis that places platypus-like ancestors before the more derived echidna species that have diverged from the platypus line in the last 80 Ma (Westerman & Edwards 1991). There is no evidence that we are aware of for a comparable evolution in vulnerable placental or marsupial mammals. Perhaps the restriction of neuronal activation to the brainstem in monotremes kept open an evolutionary path that was closed to placentals and marsupials that have forebrain as well as brainstem activation during REM sleep.

Our findings in the monotremes, echidna and platypus, have interesting implications for the evolution of REM sleep. Both animals have evidence for brainstem activation during a state with high-voltage forebrain EEG. This suggests that the forebrain aspects of REM sleep are relatively recent inventions in the mammalian line. REM sleep apparently evolved in service to the brainstem. If one assumes that an activated cortex is a requirement of dreaming, one could argue that the monotremes, although having an REM sleep-like state, do not dream.

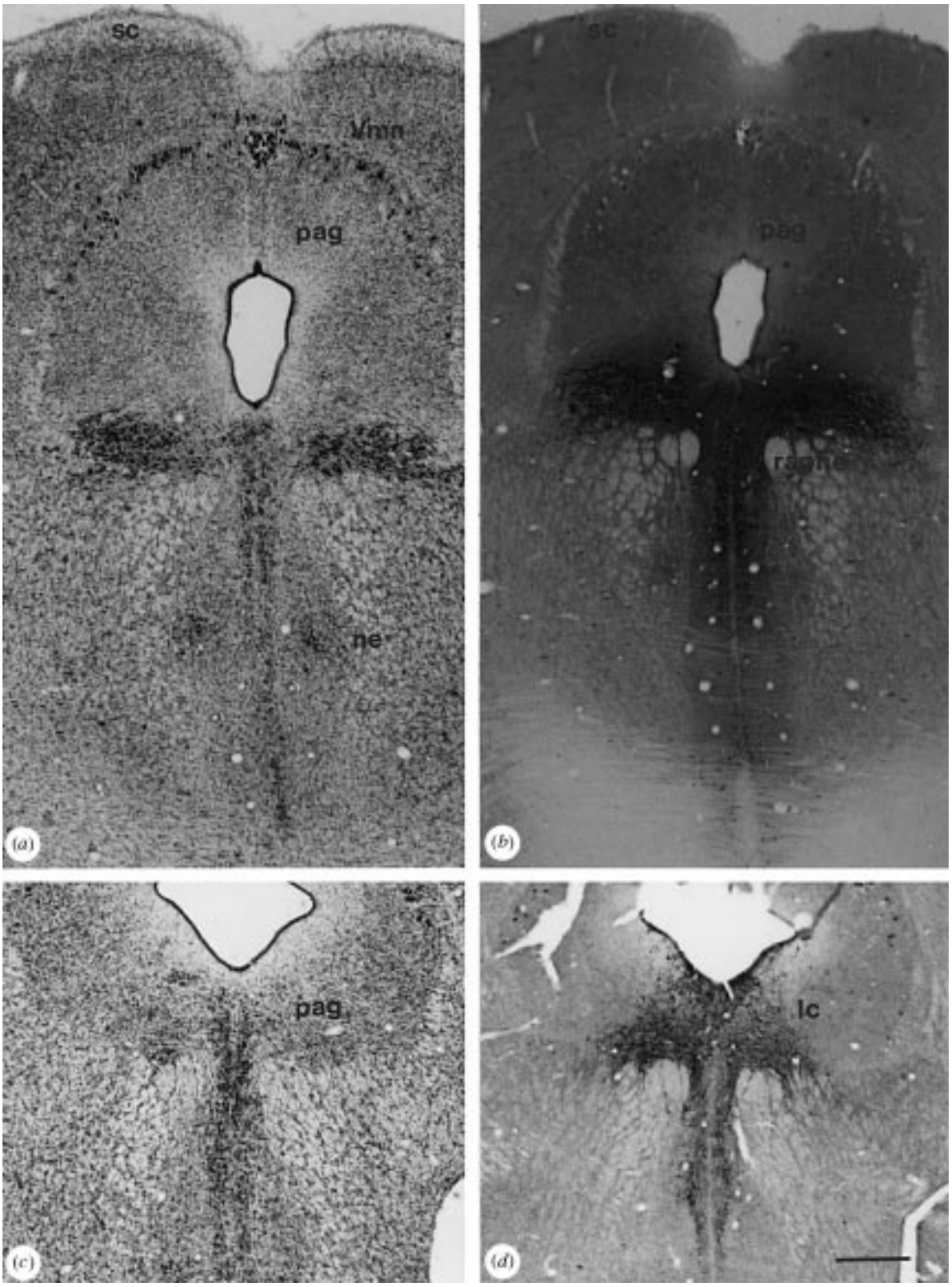

Figure 6. (*a*) Nissl stain and (*b*) immunohistochemical labelling of serotonin in the dorsal raphe nucleus in the platypus. (*c*) Nissl staining and (*d*) immunohistochemical labelling of tyrosine hydroxylase neurons in the locus coeruleus of the platypus. Pag, periaqueductal grey; Vmn, mesencephalic nucleus of the trigeminal; SC, superior colliculus.

8. ANATOMY OF THE MESOPONTINE AMINERGIC AND CHOLINERGIC CELLS IN THE PLATYPUS

It is thought that the low-voltage EEG of REM sleep is generated by brainstem projections ascending from the mesopontine region to the thalamus (Steriade *et al*. 1993). Two key cell groups that are involved are the cholinergic cells of the laterodorsal tegmental nucleus and pedunculopontine nucleus, and the noradrenergic cells of the locus coeruleus (Siegel 1994). We have used immunohistochemical staining to determine if these groups are present in the monotremes. Figures 6 and 7 show the result of our

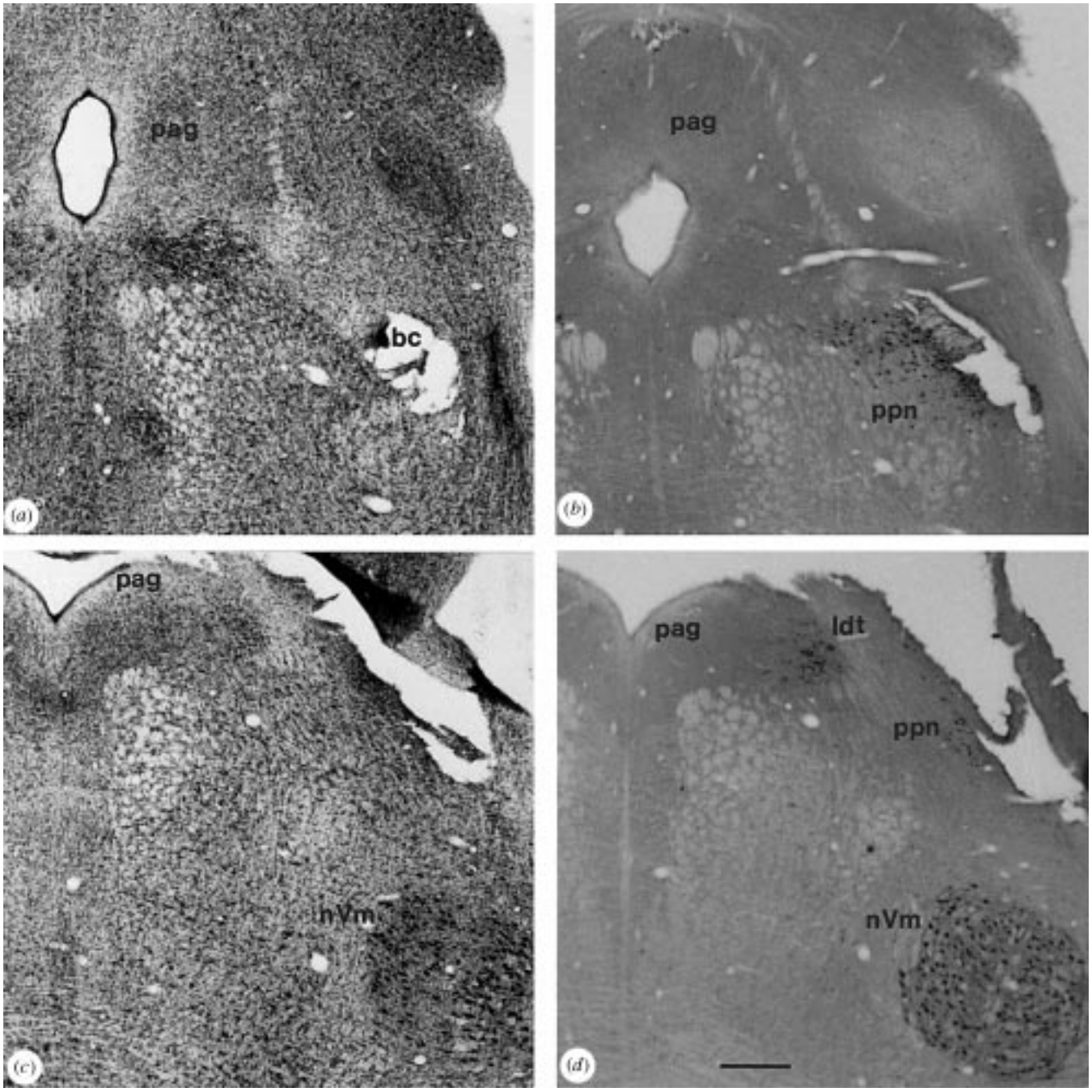

Figure 7. (*a*, *c*) Nissl stain and (*b*, *d*) immunohistochemical labelling of cholineacetyltransferase in the pedunculopontine and laterodorsal tegmental nuclei of the platypus. bc, brachium conjunctivum; ppn, pedunculopontine nucleus; ldt, laterodorsal tegmental nucleus; nVm, motor nucleus of the trigeminal.

staining in the platypus. The distribution of these cell groups does not appear to depart radically from the pattern seen in other mammals. Two questions we have not addressed are whether there is a significant ascending projection of these cells and, if so, if this projection targets the same regions as in other mammals. We would hypothesize that some critical brainstem cell group, required for the generation of the REM sleep EEG pattern and normally active during REM sleep, is either inactive or does not have the projections required for inducing EEG desynchrony in the monotremes.

Most of the echidnas' sleep period was characterized by irregular brainstem unit activity. Allison *et al*. (1972) reported $8\,\mathrm{h\,d^{-1}}$ of sleep with cortical synchrony in the echidna, a state that we found is accompanied by brainstem activation. The high amount of the 'brainstem-activated and cortex-synchronized' sleep state present in both echidna and platypus, suggest similar high amounts in the common mammalian ancestor. This indicates that this aspect of REM sleep may be ancient, predating the mammalian line. If this is so, the case for REM sleep having evolved independently in mammals and birds is considerably weakened. In the absence of evidence that the earliest mammals did not have REM sleep, it is much simpler to suppose that reptiles giving rise to both mammals and birds had REM sleep or some precursor

state. This would push the roots of REM sleep back from 150 Ma BP to approximately 250 Ma BP.

Our work with monotremes leads to several conclusions:

1. An REM sleep-like state is present in the platypus.
2. A brainstem-activated and cortex-synchronized state with some resemblance to REM sleep is present in the echidna.
3. Both the platypus and echidna show a high-voltage cortical EEG during the brainstem-activated REM-like state.

These conclusions invite further speculation:

1. The EEG activation represented by the low-voltage EEG of REM sleep evolved after the brainstem aspects of REM sleep.
2. Core aspects of the REM sleep state evolved only once, originating in the stem reptiles ancestral to mammals and birds.
3. A state with many of the aspects of REM sleep must be present in reptiles.

These last two speculations can be tested by the recording of brainstem neuronal activity in both reptiles and birds. Only in this way can we determine the nature and evolutionary history of REM sleep.

Supported by the Medical Research Service of the Veterans Administration, USPHS grant NS32819 and the Australian Research Council Special Research Centres Budget. This research was carried out according to the Australian Code of Practice for the Care and Use of Animals for Scientific Purposes under Queensland National Parks and Wildlife permit T00803 and K01782.

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