



Is there REM sleep in reptiles? A key question, but still unanswered

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REM sleep was initially described in mammals and was later found in birds. As the results obtained in reptiles were unconvincing, this suggested for years that only homeothermic species have REM sleep. However, recent studies in lizards also suggest the presence of two electrophysiological states and provide a better picture of their sleep. Nevertheless, due to differences in the expression of these states in two lizard species, as well as missing information, homology with mammalian REM sleep still could not be established. As ectotherms and homeotherms have very different physiology and neuroanatomy, we expect that, even if a state like REM sleep exists in ectotherms, its phenotypic expression should be different. Therefore, we think that a comprehensive understanding of the evolution of REM sleep will come from efforts to examine both the similarities and difference between sleep states in homeotherms and ectotherms.

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Current Opinion in Physiology 2020, 15:xx–yy

This review comes from a themed issue on **Physiology of sleep**

Edited by **A Jennifer Morton** and **Vladyslav Vyazovskiy**

<https://doi.org/10.1016/j.cophys.2020.01.001>

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Introduction

Sleep is a ubiquitous phenomenon found throughout the animal kingdom [1]. However, the division of sleep into two distinct sleep states (non-rapid eye movement (NREM) sleep and REM sleep) was often thought to be the monopoly of the homeothermic species (mammals and birds) [2]. Recent discoveries (and often forgotten old papers), however, challenged this assumption [3^{**},4^{**},5^{*}]. Besides the factual and evolutionary interest in knowing that REM sleep could be much older than expected if it is not only found exclusively in ‘warm blooded’ species, its existence in ectothermic animals, would drastically impact our view of its function(s); notably, by rejecting the hypothesis that REM sleep coevolved with thermal

genesis. This would suggest that REM sleep was not correlated with the active lifestyle of homeotherms. As the function(s) of REM sleep remains unknown, its presence or absence in ‘cold blooded’ species is crucial to determine why it exists. Therefore, this question should be addressed with the utmost care and effort to properly assess its evolution and existence across species.

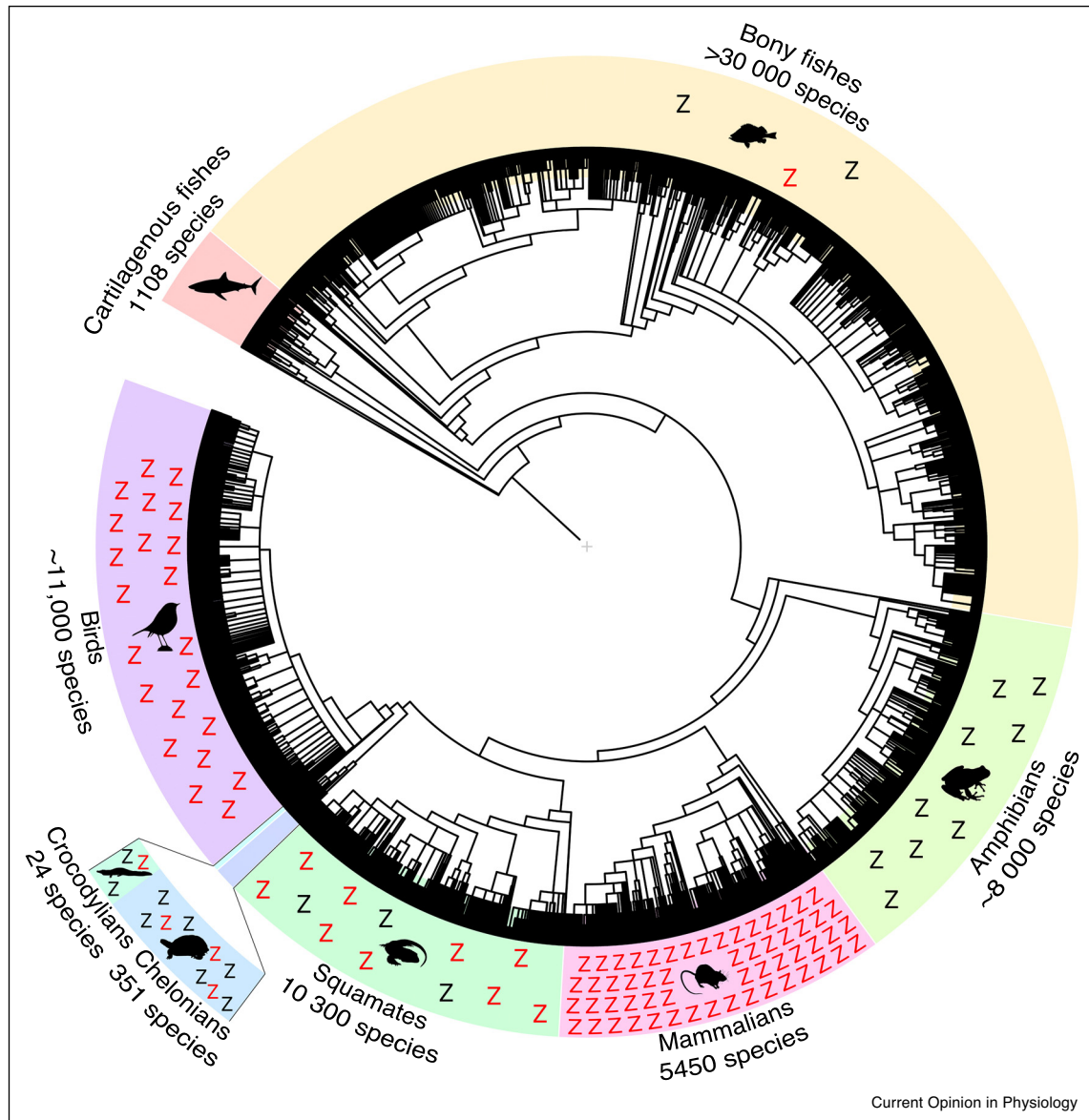
What is REM sleep? A mammalian and avian view

Before screening ectotherms for REM sleep, it is necessary to first think about what REM sleep is. Its discovery in humans and cats in the fifties was made based on the observation that eyes exhibit rapid saccades during behavioral sleep [6,7]. The activated wake-like brain activity measured via electroencephalography (EEG) during REM sleep is also one of its major features that gave REM sleep another name: paradoxical sleep [8]. During REM sleep, many physiological parameters change dramatically. The cardiac rhythm loses its regularity [9], motor automatism and twitches are frequent, thermoregulation mechanisms are turned off [10], penile erection occurs [11], brain temperature increases [12], and the cerebral blood flow also increases [13]. All of these phenomena occur while a deep muscle atonia is present in most skeletal muscle [14]. Since its discovery, multiple species have been screened to determine if they also express REM sleep. In accordance with this definition (often simplified as all the parameters were not easily accessible) a REM sleep-like state, with a wake-like EEG, rapid eye movements, and sometimes muscle atonia and muscular twitches was identified in all terrestrial mammals screened to date, as well as in all birds examined [15].

REM sleep in reptiles: what was found in the 70’s

REM sleep seems to be expressed in a similar way in mammals and birds, but what about reptiles (lizards, snakes, turtles, and crocodiles) that share a common ancestor with their homeothermic cousins? Do they express this phenomenon? This question was investigated as soon as REM sleep was discovered. Most of all the experiments were conducted on these taxa before the 80’s; but, unfortunately, those experiments failed to reach a consensus on whether reptiles exhibit REM sleep (reviewed in Ref. [16^{**}]). Indeed, as illustrated in [Figure 1](#), from those old papers around half of the studies in lizards (11 of 20 studies) reported the presence of two sleep states suggesting the existence of a putative REM sleep state [16^{**}]. Three of the 12 papers conducted on turtles and one out of the 6 on crocodylians species

Figure 1



Phylogenetic tree of the Chordata displaying the number of species studied per family; the Z icons represent the number of species recorded for sleep with electrophysiological recordings in each group. The icon is black (Z) when only one state was reported and red (Z) when two sleep states were reported (at least once, if multiple studies have been conducted in the same species). The number of species studied is based on [16^{**},54,55]. The tree was built using the 'interactive Tree Of Life (iTOL) v4' [56].

reported two sleep states [16^{**}]. Then, since the 60's, two sleep states were already reported in reptiles; however their nature still remain unclear. This is partially explained because the EEG findings vary greatly across studies, sometimes even in the same species. The findings include either no electrophysiological difference between wake and sleep, signs of one NREM sleep-like state, or two types of sleep suggestive of NREM and REM sleep (reviewed in Ref. [16^{**}]). Slow waves have rarely been reported in reptiles but isolated high-voltage sharp-waves (HShw) were often proposed as a marker of

sleep, similar to the mammalian hippocampus Sharp waves or cortical slow waves [16^{**},17^{*},18].

In reptiles, most of the studies, claiming that REM sleep (or at least a similar state to REM sleep) was present, based their conclusions on the presence of a wake-like EEG during behavioral sleep, associated with eye movements and sometimes motor automatism, seen in its mammal counterpart. In studies reporting the presence of REM sleep in reptiles, no clear muscle atonia was recorded (only four studies reported atonia over

40 [19–22]) and only one arousal threshold evaluation during putative REM sleep was conducted [23]. Thus, none of these studies were able to provide enough clues to unambiguously assert that those periods of wake-like EEG with eye movements were not short awakenings from sleep. Moreover, different brain regions were recorded, the number of individuals studied was usually small, and the ambient temperature varied across studies. All these factors might contribute to the diverse findings reported in reptiles.

Recent discoveries

The topic of REM sleep evolution recently returned to the main stage with two publications re-investigating sleep in reptiles [3**,4**] with up-to-date methods. Indeed, most of the previous recording were conducted with a polygraph, with data collected on paper. Consequently, it was difficult or impossible to apply signal processing analysis on the whole data set. Now, data digitally sampled at a high rate simultaneously from multiple brain regions and can be subject to spectral analysis across the entire recording. Digital video can also be analyzed precisely. In 2016, using modern methods silicon probes to record multisite local field potentials and unit activity combined with close up videos, Shein-Idelson *et al.* revealed that the bearded dragon (*Pogona vitticeps*) displays a period of behavioral sleep characterized by the occurrence of high amplitude sharp waves (one to two per second) in a deep brain structure, the dorsal ventricular ridge (DVR), a possible homologue of the mammalian isocortex, or claustrum-amygdala complex [24,25] (discuss below). Those periods alternated with periods of desynchronized brain activity, similar to that recorded during wakefulness in these animals [3**]. The periods with desynchronized activity were preferentially associated with eye movements (Figure 2). The two electrophysiological sleep states alternated with an almost clock-like periodicity of 80 s, never recorded before in any species (including mammals and birds). The authors concluded that those two brain activities during the sleep period of the animal were the reptile equivalent of mammalian and avian NREM and REM sleep. They also suggest that the high voltage waves found could be homologous to the hippocampal sharp waves ripple complex, an electrophysiological marker of memory processing in mammals [26]. However, as explained later, these sleep homologies are still unclear.

In 2018, we replicated those results in the bearded dragon [4**]. Although we found similar electrophysiological patterns during behavioral sleep, when we investigated sleep in a different lizard species, the Argentine tegu (*Salvator merianae*), those results painted a different story. Two sleep states were also identified in recordings from the same brain region (DVR) as in the bearded dragons. The first sleep state was characterized by the presence of isolated high amplitude waves (one every min on average)

emerging from a background pattern without a dominant rhythm. The second sleep state showed an unprecedented sustained brain oscillation at 15 Hz, not seen during wake. This oscillation was associated with isolated eye movements (Figure 2), a very slight decrease in the muscle tone, and was suppressed after the injection of a serotonin reuptake inhibitor that suppressed REM sleep in mammals and birds. Thus, in both species two electrophysiological sleep states seems to exist, but as explained later, the expressions of none of these states completely matched classical NREM sleep and REM sleep. Therefore, we do not fully agree with the current widespread idea that reptiles have REM sleep because two states were found in two species. In the next paragraph, we will discuss the pros and cons and will argue that in a comparative context the current view of REM sleep should be challenged.

Why the absence of consensus in sleeping reptiles should change our classical view of REM sleep?

The mammalian sleep traits used to identify or characterize REM sleep are sustained by the anatomy and the physiology of the animals. Thus, using those mammalian traits as a correlated of the presence or absence of REM sleep in reptiles, species that show important differences in telencephalic neuroanatomy, metabolism and lifestyle, could sometimes be puzzling. Below we will review the different features that define REM sleep in mammals and birds and discuss their existence and expression in reptiles.

Reptilian brain activity during sleep states

Most of the studies that describe sleep states from cortical EEG recordings attempt to draw comparisons with what was described in mammals. However, the cortical EEG (like any brain potential) originates from the surrounding neural tissue and is therefore shaped by its neuroanatomy and connectivity with other brain regions [27]. But, what about species, such as reptiles, with their 3-layer cortex? This peculiar cortex seems to lack the equivalent of mammalian layers II and III, the layers with extensive intracortical projections in the mammalian neocortex [28], layers that seems to play a key role in the generation of slow waves [29]. What about species that have a reduced telencephalon with a cerebellum or an optic tectum that could be more than 10 times larger than the telencephalon? Should we expect to have the same brain signature as mammals in those species? Reasonably, we might find that unlikely. Then, the absence of slow waves reported in most of the reptilian studies might simply reflect differences in neuroanatomy and connectivity.

Moreover, some reptilian studies (including the two most recent ones) recorded local field potentials (LFP), but interpreting deep brain LFP can be even more challenging than cortical EEG (Figure 2). Indeed, due to their local

nature, the LFP is even more variable across region. This was notably illustrated by the hippocampal sharp waves ripples complex, a brain oscillation associated with memory processing, that occurs during immobility, and slow wave sleep in rodent [26]. The hippocampal sharp waves ripples complex can be recorded into the *stratum radiatum* layer of hippocampus CA1 region, even though the associated ripples complex show the maximal amplitude in a different layer of CA1, the pyramidal layer [30] during NREM sleep. Thus, the only argument supporting homologies between the ‘Slow sharp’ wave recorded in the DVR in the bearded dragon and the whole brain of the Argentine tegu is their morphological similarities with their mammalian counterparts. As a consequence, to draw direct parallel from the LFP signature recorded in the lizards, functional and mechanistic study remains necessary. Without a proper understanding of the brain organization and the underlying neuronal networks responsible for this phenotype, the information obtained is circumstantial at best if it is not correlated with other physiological or behavioral changes.

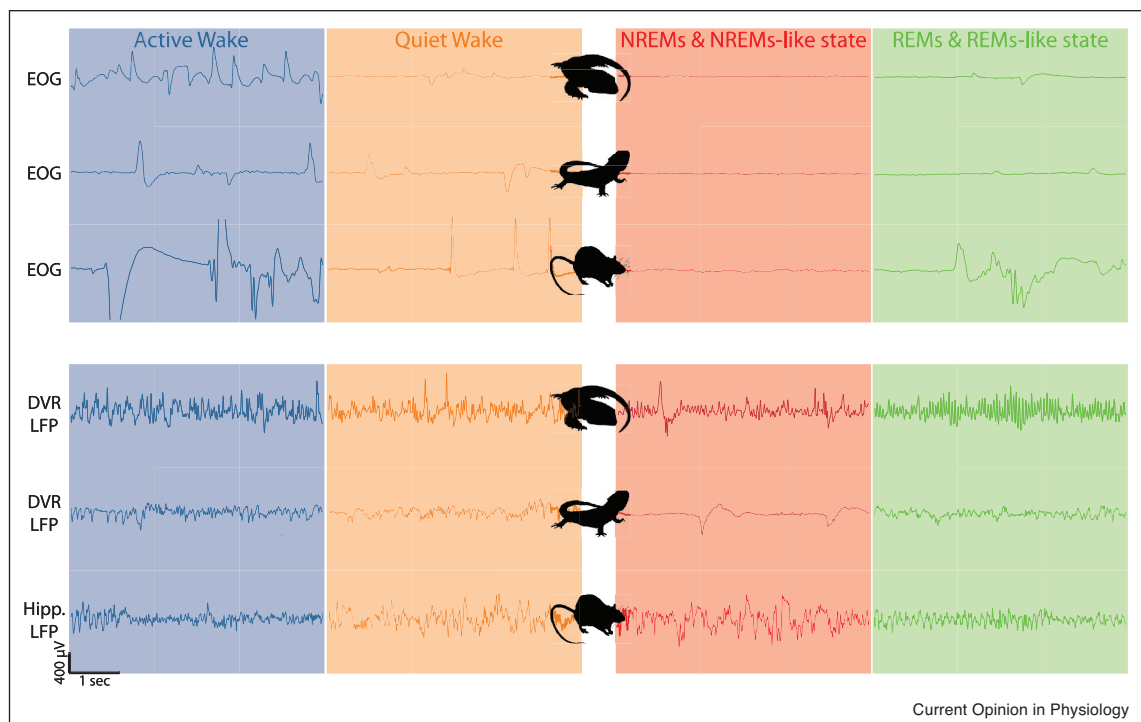
In addition to neuroanatomy, other factors, such as temperature, might influence brain activity signature and thereby complicate attempts to draw parallels with mammals. Indeed, even in mammals, it has been demonstrated

that brain temperature has an effect on the EEG; when brain temperature drops, EEG waves decrease in frequency and amplitude [31,32]. In mammals, the effect is negligible as the brain temperature is kept quite constant, but in ectotherms the brain temperature follows environmental temperature. In the wild, most reptiles are diurnal and when sleeping they are exposed to colder temperature than during the day. The difference between day and night can be more than 20°C, thus, comparing the EEG in an ectothermic species under these conditions to that of mammals is questionable. Even in lab, where reptiles were often recorded in a more controlled conditions with constant temperature, around 25°C, their brain temperature is far below that of mammals. Thus, to make true comparisons, should we compare the EEG with a mammal in hypothermia or reptiles at higher temperatures? Comparisons of this sort are likely to be meaningless, as neither condition reflects normal sleeping conditions for the species. Altogether, this show how complicated it is to draw parallels between species that do not share the same neuroanatomy and body temperature.

Sleep homeostasis

The homeostatic regulation of sleep states is one of the major features of sleep and can be assessed through depriving animals either of all sleep, or just REM sleep.

Figure 2



Selected recordings of the different vigilant states in the Argentine tegu, the bearded dragon and the brown rat. **(a)** Signals of the electro-oculogram (EOG), filtered with a low pass filter at 10 Hz, for Active Wake (blue), Quiet Wake (orange), and NREM and REM sleep and their putative equivalents for squamates in red and green, respectively. From the top to the bottom the species signals represented are from the Argentine tegu, *Salvator merianae* (Aa), the bearded dragon, *Pogona vitticeps* (Ab), and the brown rat, *Rattus norvegicus* (Ac). **(b)** Signals of the local field potential for the same states and species. DVR = Dorsal Ventricular Ridge, Hipp. = Hippocampus.

Unfortunately, in reptiles, the homeostatic regulation of putative REM sleep states has not been examined. In the Argentine tegu, after total sleep deprivation for 9 hours, the REM sleep-like state did not increase like REM sleep in mammals. However, after this 9-hours sleep deprivation, Argentine tegu's sharp waves density increased, as reported by Flanigan in turtles, crocodiles and lizards, and like the slow waves in mammals [33–35] and birds [36,37]. This tends to support the idea that reptilian sharp waves could be a marker of sleep intensity. However, data are missing to say whether they have the same role in memory processing or not. In the bearded dragon, Shein Idelson *et al.* postulated that the DVR sharp waves could be like the mammalian hippocampal Sharp Waves ripples complex. However, the fast activity observed during sharp-waves in dragons may also arise from the same processes that give rise to the fast (80–200 Hz), ripple-like, activity that occurs during the upstates that give rise to extracellular slow-waves [38]. However, no functional studies have been able to confirm this homology and the only morphological similarity is not enough to draw such parallel.

The paradox of the wake-like EEG as a necessary condition of REM sleep

In the 60's, Jouvet renamed REM sleep as paradoxical sleep because of the presence of a wake-like EEG in a sleeping animal. Since this discovery, the wake-like cortical EEG has been one of the major criteria to identify REM sleep. But in 2018, we reported a sleep state in the Argentine tegu sharing similarity with mammalian REM sleep (eye movements, reduced muscle tone, suppression after fluoxetine injection), but without wake-like LFP activity in the DVR. Instead, a sustained 15 Hz oscillation specific to this state was recorded. Does that mean that this electrophysiological pattern could not be REM sleep, as a distinct 15 Hz oscillation was not present during wake? From our point of view, a wake-like EEG should not be a necessary criterion to identify REM sleep. Indeed, REM sleep have different functions than wake and imply the recruitment of a specific neuronal network [39]. Therefore, the electrical potentials recorded in specific brain regions should differ between wake and REM sleep. Far from the stereotype, this is also the case for rodent. Indeed, when looking carefully in rats and mice, due to the hippocampal theta rhythm, the parietal EEG during REM sleep display a very singular and regular frequency at 7 Hz. As show in [Figure 2](#), this oscillation differs from the parietal EEG of an awake animal (not walking) where the frequency is more spread through the theta band (4–9 Hz).

Eye movements during sleep in reptiles?

Eye movements were associated with REM sleep since its discovery, making ocular saccades one of the major signatures of REM sleep that has been used as a marker of its existence in other species. In almost all reptile's

studies, from crocodiles to lizards and turtles, eye movements were reported during behavioral sleep suggesting the potential existence of REM sleep in reptiles [16**]. In the bearded dragon, eye movements were more frequent in the beginning of the sleep state with a wake-like LFP [3**]. Whereas in the tegu the eye movements were more frequent during the 15 Hz state. But as no arousal threshold has been conducted, it remains possible that those periods were wakefulness or at least micro-arousal. Beside this, the density of eye movements as well as their amplitude during sleep raise questions. In the bearded dragon as in the Argentine tegu, eye movements during sleep are isolated, small and do not occur in burst like they do in mammals ([Figure 2](#)). This is not related to their ocular capacity, as during wake, eye movements are more frequent, faster and larger in amplitude ([Figure 2](#)). Does that mean that REM sleep is not fully expressed in reptiles, or that this REM sleep-like state in reptiles is not homologous to mammalian REM sleep? Or that potential REM sleep functions associated with the eye movements are not as predominant in reptiles when compared to mammals? As all of these possibilities could be true, more studies of eye movements during sleep in reptiles are needed.

Phasic and tonic muscle activity during sleep state

Muscle atonia, like ocular saccades and wake-like EEG activity, is a key feature of mammalian REM sleep. But unlike the other two features, muscle atonia differentiates REM sleep from wake. In mammals, it was previously thought that atonia prevents the animal from moving when its cortex is activated (during dreaming in human). This view is still likely, but challenged, in particular by the report of dreaming without movement during NREM sleep [40,41] or the partial expression of muscle atonia in birds [42,43]. Therefore, the presence or absence of this trait in animals during a REM sleep-like state could be key to understanding whether it serves an important function of REM sleep or if it's a mammalian epiphenomenon. In reptiles, muscle tone was often recorded, but muscle atonia was seldomly reported. Even in the Argentine tegu, the tone of the deep postural muscle of the neck, during the 15 Hz oscillation, is significantly lower than during the rest of the sleep periods, the differences are very subtle and no clear atonia (like that in mammals) could be identified. This could be explained by the fact that no true muscle atonia is present during the possible homologue of REM sleep in reptiles, suggesting that in homeotherms, muscle atonia is either an epiphenomenon of REM sleep or serves a specific function related to endothermy. Another hypothesis to explain the absence of clear atonia in reptiles could be that they are always atonic during sleep. Indeed, as ectotherms, this would be consistent with their energy conservation strategy. Finally, if the muscle atonia was a core feature of the expression of mammalian and avian REM sleep, this could also mean that reptiles do not have an equivalent

REM sleep that serves the same function as in mammals and birds.

Of all the traits of REM sleep, twitching is also one of the more obvious. In neonates, REM sleep is identified mainly from this prominent feature. Twitches occurring during REM sleep are thought to play an important role in brain development [44]. Unfortunately, no clear associations between twitches and putative sleep states have been established in reptiles. Short movements of the toes and tail were reported sporadically in many studies of adult reptiles, but none (including the recent studies in the bearded dragon and the Argentine tegu) was able to clearly link those movements with any specific pattern of brain activity.

The apparent absence of a clear association between twitching and putative REM sleep states in reptiles raises several questions. Is twitching during REM sleep present only during development (*in ovo*) in reptiles as reported by Corner [45]? Or is REM sleep (defined as an active state with twitches) simply absent in reptiles? Does putative REM sleep observed in some reptiles serve the same functions as in mammals. Additional comparative and developmental work is needed to fully understand the true motor nature of REM sleep.

Sleep architecture

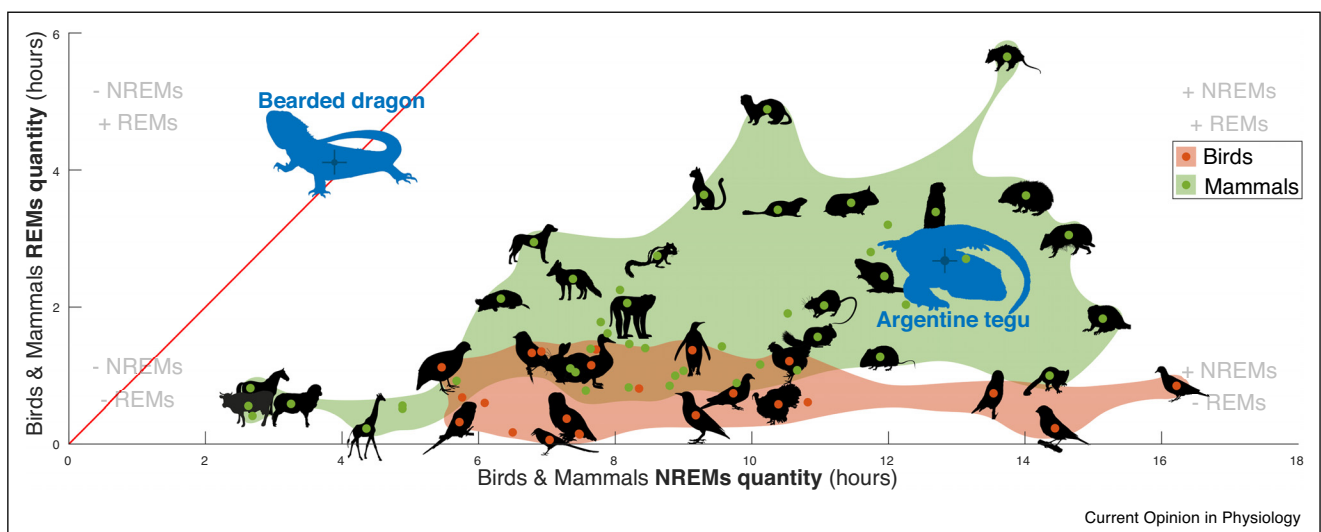
In mammals and birds, the respective quantities of NREM sleep and REM sleep vary across the development and across species (Figure 3). In addition, in birds, the duration of REM sleep episodes is much shorter,

typically only lasting between 5 to 10 s [46]. But more generally, as seen in Figure 3, the quantity of REM sleep reported in adult mammals and birds is much lower than the quantity of NREM sleep. In the bearded dragon, the putative periods of REM sleep constitute 50% of the time asleep. If this state truly does reflect REM sleep, this would mean that dragons have the greater quantity of REM sleep ever seen in adults of any animal, (excluding the platypus with its mixed sleep states [47]). This would have huge implications for our understanding of the functions of REM sleep. Indeed, such high proportions of REM sleep were only seen in neonates, supporting the developmental hypothesis of REM sleep [48,49].

The other unique aspect of the bearded dragon's sleep states is the almost perfect regularity of its sleep cycle, which is unlike that observed in any mammal or bird. Moreover, in mammals and birds, REM sleep increases in quantity progressively throughout the sleeping period. However, in the bearded dragon this is not the case.

The bearded dragon's sleep architecture not only differs from that of mammals and birds, it is also dramatically different from that observed in the Argentine tegu. In the tegu, putative REM sleep encompasses a far lower proportion of the time asleep, is more prominent at the beginning and at the end of the night, and does not occur with clock-like regularity. The duration of REM bouts is also more bird-like than that of the bearded dragon. Altogether this shows how variable sleep phenotypes are, even between two species of lizards. Finally, these differences in sleep architecture between bearded

Figure 3



Ratio of mammalian & avian REMs over NREMs compared to their putative squamates equivalents over 24 hours. The relative quantities of the two types of sleep for squamates are calculated based on the assumption for the NREMs-like state being an equivalent of the SWS and the REMs-like state the equivalent of paradoxical sleep [3**,4**]. The relative quantities were calculated based on the results found in the literature [16**,54,55]. The corners of the graph represent the minimal (–) and maximal (+) quantities of NREMs and REMs. For example, the top right corner represents the maximal quantities of both NREMs and REMs (+NREMs/+REMs).

dragons and mammals, birds, and tegus, underscore the challenges of determining homology between reptilian sleep states and those observed in homeotherms.

Others mammalian REM sleep features in reptiles

Aside from brain activity, muscle tone, and ocular activity, other traits have been reported during mammalian and avian REM sleep. Such traits should also be examined in reptiles to determine how similar the “reptilian REM sleep-like state” is to what has been found in mammals and birds.

One of those traits is the reduction of thermoregulatory responses in mammals and birds. However, as ectotherms, this trait would never be found in reptiles. Therefore, should we consider this feature of mammalian and avian REM sleep as a key component of this state? If the loss of thermoregulation mechanisms is considered a defining feature of REM sleep directly linked to its function, then it becomes clear that reptiles could not have REM sleep. However, this trait could also be a derived feature of REM sleep that appeared convergently in mammals and birds. Importantly, the presence of REM sleep in ectothermic reptiles, would then suggest that REM sleep had an initial function before its involvement in thermoregulation.

The greatest quantity of REM sleep found in young and altricial species is also a major characteristic of REM sleep, supporting its crucial role in development. Yet, even if rhythmic movements have been recorded *in ovo* in reptiles [45], this question has not been investigated using EEG recording.

Finally, another way to determine if REM sleep is present in reptiles would be to examine the neuronal network that generates and maintains REM sleep in mammals and birds. We now know that the circuitry that supports mammalian REM sleep involves multiples nuclei in the brainstem and hypothalamus. As the brainstem and diencephalic structures are highly conserved across vertebrates, all of these neuronal populations seem to be present in reptiles [50–52]. Therefore, it seems possible that reptiles possess the basic neuronal architecture required to generate REM sleep. However, as no precise brain atlases exists for reptiles, and despite one unsuccessful attempt to find a REM sleep-specific neuronal pattern in the turtle pons [53], the role of these structures in putative REM sleep in reptiles is unknown. The study of the activity and connectivity of reptilian structures involved in REM sleep in mammals is needed to draw a parallel and determine the level of homology between reptilian REM sleep-like and mammalian REM sleep.

Conclusion

The phenotypic expression of REM sleep was mainly defined from mammalian studies. Most of the traits

expressed in mammals during REM sleep were also found in birds, suggesting that both groups display a very similar state. As most of the mammalian features of REM sleep were found in birds (wake-like brain activity, atonia, ocular movements, twitches, homeostasis, absence of thermoregulation mechanisms, ontogenesis, architecture), it became obvious that REM sleep exists and, perhaps, supports the same function(s) in homeothermic species. In reptiles, things become more complex. Indeed, multiples studies from the 60's reported REM sleep in reptiles. Unfortunately, due to the high degree of similarity between REM sleep and wake, none of them convinced the scientific community. Recently, the studies in the bearded dragon and in the Argentine tegu nicely demonstrated that two sustained electrophysiological patterns exist during behavioral sleep in two different lizard species. In both cases, one sleep state was preferentially associated with eye movements (often small and isolated) than the other. However, doubts remain regarding homology between these states and mammalian and avian REM sleep. Indeed, many of the other traits associated with REM sleep in mammals (e.g. complete atonia, twitches, homeostasis, loss of thermoregulation) were not found (or not fully expressed), were not investigated or could not be expressed. Further adding to the challenges of interpreting the evolutionary implications of the research on sleep in reptiles, is the finding that the expression of putative REM sleep states differs dramatically between two species of lizards studied using the same methods in the same laboratory. Therefore, it is still unclear whether reptiles have a mammalian REM sleep like state (sharing the same function) but differently expressed, if they have a partial mammalian REM sleep-like state or if they have another sleep state supporting other functions. Although our ultimate aim is to gain understanding about REM sleep in mammals, through tracing its evolution, we strongly believe that in addition to the similarities, the differences between putative REM sleep in reptiles and mammalian REM sleep should be given equal attention when studying reptiles. Indeed, because of the specific physiology and neuroanatomy of reptiles we believe that we should not expect that most of the mammalian REM sleep traits will be present in reptiles. To our point of view, the only way to understand the evolutionary history of REM sleep is to conduct more studies in additional species, and to investigate the other main traits of mammalian REM sleep, like its ontogenesis, homeostasis, neuronal basis . . . Our understanding of REM sleep will come from our emancipation from its mammalian expression. Recent very high quality studies promote the existence of REM sleep in reptiles, and even fishes [5^{*}], seemingly pushing the origin of this state further back in time. However, we should be cautious about reaching simple clear-cut conclusions about the evolution of REM sleep that fail to incorporate the differences between species. Indeed, we strongly believe that the differences between mammals, birds, and reptiles, as well as between

reptilian species, may prove to be a rich resource for examining the evolution and functions of REM sleep. This more genuine comparative approach will likely yield a more comprehensive understanding than one that attempts to force reptilian sleep states to fit within the template used to define mammalian REM sleep.

REM sleep is a phenotypic expression of a singular, mammalian state also found in birds. Just like mammals have a hairy skin and birds a feathery skin, reptiles have a scaled skin. All skins protect the animal from infection, but, in mammals and birds, it also provides a high level of thermal insulation. Just like skin, REM sleep could have different species related phenotypes and could serve common and specific functions. Therefore, we will understand its nature and functions by studying its phenotypic variability across species, not by trying to dress it in mammalian clothes.

Conflict of interest statement

Nothing declared.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.cophys.2020.01.001>.

References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- of special interest
- of outstanding interest

1. Nath RD, Bedbrook CN, Abrams MJ, Basinger T, Bois JS, Prober DA, Sternberg PW, Gradinaru V, Goentoro L: **The jellyfish *Cassiopea* exhibits a sleep-like state.** *Curr Biol* 2017, **27**:2984-2990.e3.
2. Kavanau JL: **REM and NREM sleep as natural accompaniments of the evolution of warm-bloodedness.** *Neurosci Biobehav Rev* 2002, **26**:889-906.
3. Shein-Idelson M, Ondracek JM, Liaw H-P, Reiter S, Laurent G:
 - **Slow waves, sharp waves, ripples, and REM in sleeping dragons.** *Science* 2016, **352**:590-595.
 This paper show for the first time the existence of two distinct brain activities during the behavioral sleep of the lizard, *Pogona vitticeps*.
4. Libourel P-A, Barrillot B, Arthaud S, Massot B, Morel A-L, Beuf O,
 - Herrel A, Luppi P-H: **Partial homologies between sleep states in lizards, mammals, and birds suggest a complex evolution of sleep states in amniotes.** *PLoS Biol* 2018, **16**:e2005982.
 This study replicates the data obtained from Ref. [3] and manages to record sleep in a new species of lizard, *Salvator merianae*. This paper demonstrates, that despite the presence of two electrophysiological sleep states in both species, the similarities with mammalian sleep states are not so straight forward in both lizard species.
5. Leung LC, Wang GX, Madelaine R, Skariah G, Kawakami K,
 - Deisseroth K, Urban AE, Mourrain P: **Neural signatures of sleep in zebrafish.** *Nature* 2019, **571**:198-204.
 This work offers a new approach to polysomnographic recording. This study reported two brain signatures during resting in restrained juvenile zebrafish.
6. Aserinsky E, Kleitman N: **Regularly occurring periods of eye motility, and concomitant phenomena, during sleep.** *Science* 1953, **118**:273-274.
7. Dement W: **The occurrence of low voltage, fast, electroencephalogram patterns during behavioral sleep in the cat.** *Electroencephalogr Clin Neurophysiol* 1958, **10**:291-296.
8. Jouvet M, Michel F, Courjon J: **On a stage of rapid cerebral electrical activity in the course of physiological sleep.** *C R Seances Soc Biol Fil* 1959, **153**:1024-1028.
9. Snyder F, Hobson JA, Morrison DF, Goldfrank F: **Changes in respiration, heart rate, and systolic blood pressure in human sleep.** *J Appl Physiol* 1964, **19**:417-422.
10. Parmeggiani PL: **Thermoregulation and sleep.** *Front Biosci* 2003, **8**:s557-567.
11. Schmidt MH, Valatx JL, Schmidt HS, Wauquier A, Jouvet M: **Experimental evidence of penile erections during paradoxical sleep in the rat.** *Neuroreport* 1994, **5**:561-564.
12. Parmeggiani PL, Zamboni G, Perez E, Lenzi P: **Hypothalamic temperature during desynchronized sleep.** *Exp Brain Res* 1984, **54**:315-320.
13. Bergel A, Deffieux T, Demené C, Tanter M, Cohen I: **Local hippocampal fast gamma rhythms precede brain-wide hyperemic patterns during spontaneous rodent REM sleep.** *Nat Commun* 2018, **9**:5364.
14. Jouvet M, Michel F: **Electromyographic correlations of sleep in the chronic decorticate & mesencephalic cat.** *C R Seances Soc Biol Fil* 1959, **153**:422-425.
15. Campbell SS, Tobler I: **Animal sleep: a review of sleep duration across phylogeny.** *Neurosci Biobehav Rev* 1984, **8**:269-300.
16. Libourel P-A, Herrel A: **Sleep in amphibians and reptiles: a review and a preliminary analysis of evolutionary patterns: Sleep in amphibians and reptiles.** *Biol Rev* 2016, **91**:833-866.

This paper is a non-exhaustive review of the work that was conducted in the field of sleep research in amphibians and reptiles. This review reports the variability of the results obtained from reptiles and discuss the absence of consensus on the presence of REM sleep in this group.
17. Tisdale RK, Lesku JA, Beckers GJL, Rattenborg NC: **Bird-like propagating brain activity in anesthetized Nile crocodiles.** *Sleep* 2018, **41**.

This study demonstrates the existence of propagating waves in the anesthetized brain of a species of crocodile, *Corcodylus niloticus*, and proposes them as an ancestral form of the mammalian and avian slow wave.
18. Hartse KM: **Sleep in insects and nonmammalian vertebrates.** In *Principles and Practice of Sleep Medicine*. Edited by Kryger MH, Roth TC, Dement WC. Elsevier; 1994:95-104.
19. Vasilescu E: **Sleep and wakefulness in the tortoise *Emys orbicularis*.** *Rev Roum Biol Ser Zool* 1970, **15**:177-179.
20. Rechtschaffen A, Bassan M, Ledecy-Janecek S: **Activity patterns in *caiman sclerops*.** *Psychophysiology* 1968, **5**:201.
21. Huntley A, Donnelly M, Cohen H: **Sleep in the desert iguana, *Dipsosaurus dorsalis*.** *Sleep Res* 1977, **6**:143.
22. Peyrethon J, Dusan-Peyrethon D: **Polygraphic study of the sleep-wake cycle in 3 genres of reptiles.** *C R Seances Soc Biol Fil* 1969, **163**:181-186.
23. Ayala-Guerrero F, Mexicano G: **Sleep and wakefulness in the green iguanid lizard (*Iguana iguana*).** *Comp Biochem Physiol A Mol Integr Physiol* 2008, **151**:305-312.
24. Tosches MA, Yamawaki TM, Naumann RK, Jacobi AA, Tushev G, Laurent G: **Evolution of pallium, hippocampus, and cortical cell types revealed by single-cell transcriptomics in reptiles.** *Science* 2018, **360**:881-888.
25. Aboitiz F: **Comparative development of the mammalian isocortex and the reptilian dorsal ventricular ridge. Evolutionary considerations.** *Cereb Cortex N Y N* 1991, **9**:783-791.
26. Buzsáki G: **Hippocampal sharp wave-ripple: a cognitive biomarker for episodic memory and planning: HIPPOCAMPAL SHARP WAVE-RIPPLE.** *Hippocampus* 2015, **25**:1073-1188.

27. Buzsáki G, Anastassiou CA, Koch C: **The origin of extracellular fields and currents – EEG, ECoG, LFP and spikes.** *Nat Rev Neurosci* 2012, **13**:407-420.
28. Reiner A: **Neurotransmitter organization and connections of turtle cortex: implications for the evolution of mammalian isocortex.** *Comp Biochem Physiol A Physiol* 1993, **104**:735-748.
29. Sanchez-Vives MV, McCormick DA: **Cellular and network mechanisms of rhythmic recurrent activity in neocortex.** *Nat Neurosci* 2000, **3**:1027-1034.
30. Ylinen A, Bragin A, Nadasdy Z, Jando G, Szabo I, Sik A, Buzsáki G: **Sharp wave-associated high-frequency oscillation (200 Hz) in the intact hippocampus: network and intracellular mechanisms.** *J Neurosci* 1995, **15**:30-46.
31. Deboer T: **Brain temperature dependent changes in the electroencephalogram power spectrum of humans and animals.** *J Sleep Res* 1998, **7**:254-262.
32. ten Cate J, Horsten GPM, Koopman LJ: **The influence of the body temperature on the EEG of the rat.** *Electroencephalogr Clin Neurophysiol* 1949, **1**:231-235.
33. Flanigan WF: **Sleep and wakefulness in chelonian reptiles. II. The red-footed tortoise, *Geochelone carbonaria*.** *Arch Ital Biol* 1974, **112**:253-277.
34. Flanigan WF: **Sleep and wakefulness in iguanid lizards, *Ctenosaura pectinata* and *Iguana iguana*.** *Brain Behav Evol* 1973, **8**:401-436.
35. Flanigan WF, Wilcox RH, Rechtschaffen A: **The EEG and behavioral continuum of the crocodylian, *Caiman sclerops*.** *Electroencephalogr Clin Neurophysiol* 1973, **34**:521-538.
36. Rattenborg NC, Martinez-Gonzalez D, Lesku JA: **Avian sleep homeostasis: convergent evolution of complex brains, cognition and sleep functions in mammals and birds.** *Neurosci Biobehav Rev* 2009, **33**:253-270.
37. Lesku JA, Vyssotski AL, Martinez-Gonzalez D, Wilzeck C, Rattenborg NC: **Local sleep homeostasis in the avian brain: convergence of sleep function in mammals and birds?** *Proc R Soc B Biol Sci* 2011, **278**:2419-2428.
38. Grenier F, Timofeev I, Steriade M: **Focal synchronization of ripples (80-200 Hz) in neocortex and their neuronal correlates.** *J Neurophysiol* 2001, **86**:1884-1898.
39. Luppi P-H, Clément O, Sapin E, Gervasoni D, Peyron C, Léger L, Salvert D, Fort P: **The neuronal network responsible for paradoxical sleep and its dysfunctions causing narcolepsy and rapid eye movement (REM) behavior disorder.** *Sleep Med Rev* 2011, **15**:153-163.
40. Cavallero C, Cicogna P, Natale V, Occhionero M, Zito A: **Slow wave sleep dreaming.** *Sleep* 1992, **15**:562-566.
41. Siclari F, Bernardi G, Cataldi J, Tononi G: **Dreaming in NREM Sleep: a high-density EEG study of slow waves and spindles.** *J Neurosci Off J Soc Neurosci* 2018, **38**:9175-9185.
42. Dewasmes G, Cohen-Adad F, Koubi H, Le Maho Y: **Polygraphic and behavioral study of sleep in geese: existence of nuchal atonia during paradoxical sleep.** *Physiol Behav* 1985, **35**:67-73.
43. Rattenborg NC, van der Meij J, Beckers GJL, Lesku JA: **Local aspects of avian non-REM and REM sleep.** *Front Neurosci* 2019, **13**.
44. Blumberg MS, Coleman CM, Gerth AI, McMurray B: **Spatiotemporal structure of REM sleep twitching reveals developmental origins of motor synergies.** *Curr Biol* 2013, **23**:2100-2109.
45. Corner MA: **Sleep and the beginnings of behavior in the animal kingdom—studies of ultradian motility cycles in early life.** *Prog Neurobiol* 1977, **8**:279-295.
46. Lesku JA, Meyer LCR, Fuller A, Maloney SK, Dell’Omo G, Vyssotski AL, Rattenborg NC: **Ostriches sleep like platypuses.** *PLoS One* 2011, **6**:e23203.
47. Siegel JM, Manger PR, Nienhuis R, Fahringer HM, Shalita T, Pettigrew JD: **Sleep in the platypus.** *Neuroscience* 1999, **91**:391-400.
48. Roffwarg HP, Muzio JN, Dement WC: **Ontogenetic development of the human sleep-dream cycle.** *Science* 1966, **152**:604-619.
49. Del Rio-Bermudez C, Blumberg MS: **Active sleep promotes functional connectivity in developing sensorimotor networks.** *BioEssays News Rev Mol Cell Dev Biol* 2018, **40**:e1700234.
50. Ayala-Guerrero F, Mexicano G: **Topographical distribution of the locus coeruleus and raphe nuclei in the lizard *Ctenosaura pectinata*: functional implications on sleep.** *Comp Biochem Physiol A Mol Integr Physiol* 2008, **149**:137-141.
51. Cardot J, Fellmann D, Bugnon C: **Melanin-concentrating hormone-producing neurons in reptiles.** *Gen Comp Endocrinol* 1994, **94**:23-32.
52. Butler AB, Hodos W: *Comparative Vertebrate Neuroanatomy: Evolution and Adaptation.* Wiley-Interscience; 2005.
53. Eiland MM, Lyamin OI, Siegel JM: **State-related discharge of neurons in the brainstem of freely moving box turtles, *Terrapene carolina major*.** *Arch Ital Biol* 2001, **139**:23-36.
54. Capellini I, Barton RA, McNamara P, Preston BT, Nunn CL: **Phylogenetic analysis of the ecology and evolution of mammalian sleep.** *Evolution* 2008, **62**:1764-1776.
55. Roth TC, Lesku JA, Amlaner CJ, Lima SL: **A phylogenetic analysis of the correlates of sleep in birds.** *J Sleep Res* 2006, **15**:395-402.
56. Letunic I, Bork P: **Interactive Tree Of Life (iTOL) v4: recent updates and new developments.** *Nucleic Acids Res* 2019, **47**:W256-W259.