THE BIRTH OF THE MAMMALIAN SLEEP

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Summary

The Nocturnal Bottleneck explains how mammals evolved from their reptilian ancestors after inverting the chronotype, form diurnal to nocturnal. Pre-mammals traded-off the excellent visual system of their ancestors for improvements in audition and in olfactory telencephalon, needed for efficient orientation in the dark. This was how the mammalian nocturnal telencephalic wakefulness was born.

However, the modified visual system of those pre-mammals became sensitive to the dangerous diurnal light and the exposure would involve a high risk of blindness and death. Therefore, pre-mammals had to remain immobile with closed eyes hidden in lightproof burrows during light time. This was the birth of the mammalian sleep.

Typical reptiles distribute their wake time cycling between Basking Behavior, to attain the preferred body temperature, and poikilothermic Goal Directed Behavior, to perform life sustaining tasks. These cycles persisted during the new mammalian sleep. However, as the behavioral output had to be blocked during light time, the paralyzed reptilian Basking Behavior and Goal Directed Behavior cycles became the NREM and REM cycles, respectively. This was how NREM and REM cycles remained incorporated within the mammalian sleep.

After the Cretaceous-Paleogene extinction, the environmental pressure for nocturnal life was softened, allowing high variability in chronotype and sleeping patterns. This permitted some mammalian groups, e.g., primates, to begin the quest for diurnal wake.

Concluding, sleep constituted an additional bottleneck in the mammalian evolution. The reduced population of pre-mammals that was able to develop sleep during light time, including NREM and REM, became full mammals and survived; the remainder perished.

Keywords: Evolutionary bottleneck, Evolution of sleep, Sleep variability, Sleep function.

1. Introduction

The mysterious nature of sleep has been repeatedly affirmed. Indeed, we ignore the answer to many important sleep-related questions. Among others, we ignore why we sleep, why sleep is an active process, and why two sleep phases exist.

It is generally recognized, however, that the answer to these questions would be immediately understood if we would know, with precise details, how sleep evolved. Many reports attempted disclosing the evolution of sleep but, for the time being, most were incomplete and left some important facts unexplained. We have reviewed ten recent reports (since 2016) dealing with the evolution of sleep. Eight out of them (Miyazaki et al., 2017; Blumberg & Rattenborg, 2017; Joiner, 2016; Ungurean et al., 2019; Anafi et al., 2019; Kashiwagi and Hayashi, 2020; Hayashi & Liu., 2017; Blumberg and Rattenborg, 2017) accepted the presence of behavioral sleep in poikilothermic vertebrates and invertebrates. Regarding the remainder, one was eclectic, simply demanding for non-homeothermic animals the same rigorous methods used for ascertaining sleep in mammals and, vice-versa, applying to mammals the molecular techniques developed in invertebrates (Hartse, 2017). The last one (Aristakesyan, 2016) only referred the vertebrate sleep, recognizing therefore the existence of primitive behavioral sleep in poikilothermic vertebrates and assuming therefore the evolutionary continuity of sleep in the vertebrate phylum. Hopefully, the present review will shed light first, on the monophyletic or polyphyletic nature of animal sleep and second, on explaining that sleep appeared in mammals because of an evolutionary bottleneck that forced, in their reptilian ancestors, a change in chronotype, from diurnal, to nocturnal. This change facilitated the loss of the mechanisms protecting the eye against the dangers of diurnal bright light, which in turn, provoked the emergence of active sleep during light time (Rial et al, 2019).

2. Phylogeny of mammals. The nocturnal bottleneck

Extant Mammals comprise Prototheria (monotremes), Metatheria (marsupials) and Eutheria (placental). They constitute a monophyletic group that arose in or before the Early Jurassic, about ~200 Million Years Ago (Ma) (Kielan-Jaworowska et al., 2005). Mammals evolved from small sized Mesozoic synapsids (Bakker, 1971; Kemp, 2005) that, as modern reptiles, were dependent on solar heat to warm their body. We will see that some descendants of the primitive reptilian stock began developing endothermic metabolism, so being able in extending their activity, first to crepuscular hours and, after developing full endothermy, to the entire night. Simultaneously, their sensory system, their behavior and the corresponding neural controlling networks became adapted to nocturnal life.

These changes are currently attributed to the Nocturnal Evolutionary Bottleneck (NEB) that was first proposed by Walls (1942). An evolutionary bottleneck is defined as an event that drastically reduces the size of a population and allows survival of only those showing a reduced specific number of genes (Chakraborty & Kimmel, 2001). In the case of the NEB, Walls observed numerous adaptations to nocturnal vision in the eyes of modern mammals, irrespective of their current chronotype. He concluded that mammals evolved from reptiles because of a prolonged (over 100 Ma) nocturnal phase that was facilitated by the absence of small sized competitors during nighttime and, in contrast, was forced by the competition with the big sized ectothermic dinosaurs that occupied the diurnal niche. After Walls, many authors provided confirmatory evidence for the NEB hypothesis (Gerkema et al., 2013; Heesy & Hall, 2010; Maor et al., 2017; Wu et al., 2017) and, to our knowledge, it remains unchallenged. Furthermore, it is believed that only after the Cretaceous–Paleogene (K–Pg) mass extinction event (about 66 Ma) (Elewa, 2008, Witts et al., 2016; Canudo et al., 2016), the mammalian radiation was possible (Close et al., 2015; Meredith et al., 2011; O'Leary et al., 2013) and some orders (e.g., some primates) began the quest for crepuscular or diurnal activity.

The following paragraphs will describe how pre-mammals developed endothermic metabolism, adapted their main sensorial systems to nocturnal activity and promoted, possibly, the diurnal sleep.

3. How reptiles developed endothermic metabolism

It is believed that basal reptiles, possessed the capacity to develop the basic cardiovascular and metabolic mechanisms for endothermic generation of heat (Tattersall, 2016). They developed subcutaneous lipid layers providing thermal isolation (Frair et al., 1972; Davenport et al., 1990) that was furtherly improved by developing, in early mammals, hairy epithelial tegument (Martin et al., 2015) concomitantly with sweating and milk secreting glands (Lefèvre et al., 2010). Modern reptiles also possess heat saving countercurrent vasculature in the limbs (Greer et al., 1973) and may use the muscular activity to increase the production of endogenous heat (Clarke & Pörtner, 2010; Greer et al., 1973). It has been thus affirmed that the thermoregulatory difference between reptiles and mammals is mostly quantitative and not qualitative (Grigg et al., 2004). In fact, some extant turtles can maintain a high Body Temperature (BT) while submerged in cool water (Frair et al., 1972; Davenport et al., 1990) and tegu lizards may increase their BT during the reproductive season to extend the activity to crepuscular and dark time (Tattersall, 2016).

Nevertheless, the reptiles that gave origin to mammals - as well as modern ones - are basically dependent on external sources of heat and heliothermic behavior (Garrick, 2008). Therefore, according to the Q_{10} law, the reptilian metabolism and BT normally descend during nighttime and their physiological activity and behavior is correspondingly reduced. The Q_{10} index represents the ratio of the velocity of a given physiological process versus the same process at a temperature 10 °C lower. Typical values of the Q_{10} oscillate around 2, meaning that every 10 ºC descent in BT halves the speed of the process under consideration (Bennett, 1984).

An important consequence of the Q_{10} effect is that, being impossible the behavioral control of BT during nighttime, what is currently called “reptilian sleep” is a passive and cooled state of reduced physiological performance, quite different from the mammalian sleep (Rial et al., 2010) which, contrasting, is an active state (Hobson, 1989). This fact has important consequences on the significance of some recent studies searching REM and NREM sleep in supposedly sleeping pogona and tegu lizards (Shein-Idelson et al., 2016, Libourel et al., 2018). Although a more recent study (Libourel & Barrillot, 2020) reduced the significance of these reports, their errors continue, because they ignored that our group described, many years ago, the origin of NREM and REM cycles (Nicolau et al., 2000; Rial et al., 2000, 2010) a proposal that, at present, remains unrebutted. In these reports, we explained how the Basking Behavior (BB) and the Goal Directed Behavior (GDB) of waking reptiles gave origin to the mammalian NREM sleep and REM sleep, respectively.

4. How reptiles adapted their sensory systems to nighttime

The mammalian ancestors were sight-oriented reptiles, with well-developed eyes, sophisticated tetrachromatic color vision and capacity for fine visual analysis (Bowmaker, 1998; Collin, 2009). However, the light of high intensity may be harmful for retinal cells (De Vera Mudry et al., 2013), even in the wavelengths of maximal absorption of retinal pigments (Anderson et al., 1972; Organisciak et al., 1992; Wasowicz et al., 2002; Marco-Gomariz et al., 2006). For instance, despite being well protected against high light intensities, actinic keratosis, cataracts and retinal degenerations are common conditions in humans (Taylor, 1989; Cruickshanks et al., 1993; Sui et al., 2013; Jacobs, 2015; Taylor et al., 1992). These effects should have been aggravated in those nocturnal pre-mammals that, pursuing the highest visual sensitivity - needed to conquer nighttime - abandoned the mechanisms that protected their eyes and retina from photo oxidation (Jacobs, 2015; Taylor et al., 1992; Ringvold et al. 1998). As the chromatic discrimination is unnecessary in dark environments, it was also abandoned. In consequence, early mammals were - and many modern ones still are (Gerkema et al., 2013) - nocturnal, dichromatic (Sui et al., 2013) and, in some species, monochromatic (Peichl, 2005). Summarizing, the full set of protective mechanisms present in the eyes of diurnal reptiles, as well as their high visual acuity, spatial resolution and chromatic capabilities, were traded-off by increases in sensitivity. They incurred, however, in high susceptibility to the dangers of diurnal light (Gerkema et al., 2013; Heesy & Hall, 2010) and, in the case of accidental exposure, risked blindness, with the consequent death and extinction. Indeed, irreversible retinal damage has been observed after exposure to 60 lux during light time in pigmented rats and to 20–25 lux in albino rats (Marco-Gomariz et al., 2006; Wasowicz et al., 2002).

The reductions in visual performance were compensated by developing alternatives for orientation in the dark. The auditory sensitivity was greatly increased after modifying the reptilian articulation of the jaw, relocating the residual bones, malleus, incus and stapes, in the middle ear. This also extended the audition to high frequency ranges (Allin, 1975; Crompton & Parker, 1978). The development of the ear pinnae, with its motor control, allowed locating the precise origin of sounds and the capacity to follow the movement of the sound sources (Grothe & Pecka, 2014; Coleman & Boyer, 2012). Furtherly, the development of the mystacial vibrissae allowed the “face touch”, improving the exploration in the dark (Muchlinski et al., 2013).

The skull endocasts of successive pre-mammals show continuous size increase in olfactory bulbs (Zelenitsky et al., 2011), which was correlated with increased telencephalic and cerebellar size (Northcutt, 2011; Rowe & Shepherd, (2016). The improvement of olfaction, needed for orientation in the dark, imposed high demands in computational power for creating and memorizing precise navigational maps to find foods, recognizing dangers, friends and relatives and is currently considered capital for the development of the distinctive mammalian isocortex (Allman, 1990; Aboitiz & Montiel, 2015). These lines are only a short review on the main physiological changes needed to become adapted to night life and prepared the field for describing the development of sleep in primitive mammals.

5. The birth of the mammalian sleep

An on-off switch exists in the reptilian hypothalamus, with warm- and cool-sensitive neurons that control immobility during cool-dark time and activity during warm-light time (Berk & Heath, 1976; Bicego et al., 2007; Kluger et al., 1973; Hammel et al., 1967). As the BT of poikilothermic animals is strictly dependent on environmental temperature, the hypothalamic switch is safe enough to guarantee a correct chronotype and could never be wrong, for instance promoting activity during cool-dark time. However, when pre-mammals began homeothermy, the constancy in BT would easily fool the switch and, in the case of failure, they would have been at risk of exposure to daylight, which, possibly, could cause blindness and the consequent extinction. Only survived the few ones that improved the hypothalamic warm/cool switch by substituting the main zeitgeber, from temperature, as normal in reptiles, to light, the basic mammalian zeitgeber (Ellis et al., 2009). Indeed, when early mammals reached a stable BT, the span of perceived thermic oscillations would have been reduced, posing at risk the organization of the rest-activity circadian cycles. Thus, using the light-dark daily oscillations as the main zeitgeber, signified a significant improvement in the adaption to homeothermy and in the safety of the circadian control.

Those pre-mammals also suffered a high environmental pressure for converting the hypothalamic switch into a bi-stable switch, so obtaining additional increases in sleep stability and facilitating survival. Most likely, this was how the so-called sleep Flip-Flop (Saper et al., 2001) appeared, coupled to two neuronal ensembles: a set of sleep motor neurons and another set of wakefulness promoting neurons, interconnected through mutually inhibitory fibers (Bringmann, 2018).

Considering that the consequences of the NEB lasted over 100 million years, those pre-mammals had plenty of time for the described transformations: for endothermic metabolism, for dark-adapted chronotype, for the hypothalamic developing the light/dark bi-stable switch and, in sum, from diurnal activity to diurnal active sleep.

However, the transformation of the diurnal reptilian wakefulness into the mammalian diurnal sleep conserved, most likely, the two basic behavioral patterns of the reptilian waking: the thermoregulatory Basking Behavior (BB) and the Goal Directed Behavior (GDB) in which the thermoregulation is discarded, just as occurs during NREM and REM, respectively. To guarantee rest, however, the output of both BB and GDB had to be paralyzed (Nicolau et al., 2000; Rial et al., 2010). BB was paralyzed after developing a group of inhibitory cells in the substantia nigra, pars reticulata, that in modern mammals is responsible of blocking the NREM behavioral output (Liu et al., 2020), while a group of glycinergic-GABAergic neurons of the rostroventral medulla were developed to provoke the REM muscular atonia (Sakai et al., 1979; Lai & Siegel, 1988; Morales et al., 2006; Vetrivelan et al., 2009). So, NREM and REM are paralyzed versions of BB and GDB, respectively (Nicolau et al., 2000; Rial et al., 2007, 2010, 2018).

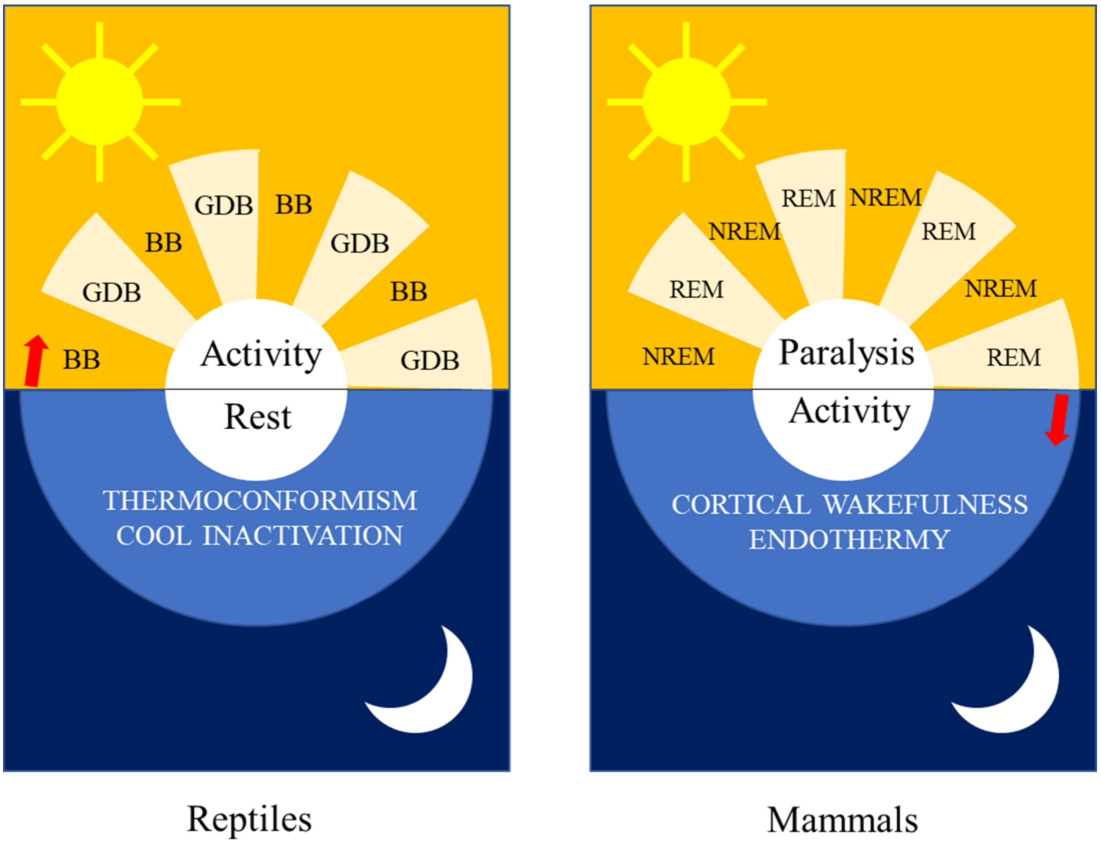

Figure 1. A day in the life of a reptile (left) and a mammal (right). In reptiles, activity begins shortly after dawn (left red up arrow), when the environmental temperature approaches the preferred one. Then, the animal begins cycling between basking (BB) and Goal Directed Behavior (GDB) until approaching dark time, when the animal search a safe burrow to enter in cool rest. In nocturnal mammal's, life begins after sundown (right red down arrow) with endothermic activity that is maintained through the whole day. However, activity is suspended on arrival of light time when nocturnal mammals enter in NREM-REM sleep cycles.

Transforming the reptilian wake into mammalian sleep, while maintaining – paralyzed - the two reptilian states, was the simplest option to escape from the dangers of diurnal light. Those animals had to remain immobile with closed eyes in light-proof burrows during the illuminated period (~12 h daily) but this was also the mechanism, perhaps unintended, to integrate NREM and REM within modern sleep (figure 1). By the way, what was essentially new in mammals was not sleep, but the cortical wakefulness. In fact, the mammalian nocturnal wake was a new state under control of the newly developed telencephalic cortex, with no antecedent in poikilothermic vertebrates (De Vera et al., 1993; Nicolau et al., 2000; Rial et al., 2007, 2010, 2018). Furtherly, these transformations allow, at present, responding a basic question: which was the function of that newly developed diurnal sleep? The evident answer is that early mammals slept to rest, so avoiding blindness and the consequent extinction.

Noteworthy, the described processes constituted a second evolutionary bottleneck. The first one, the Walls' NEB, only explains that a small group of early mammals survived after becoming adapted to nocturnal life. This adaptation was, however, insufficient; the survivors were immediately submitted to a second evolutionary bottleneck: only those capable of inventing sleep during light time survived. Therefore, sleep constituted a second bottleneck encapsulated within the primary NEB.

6. The variability in the traits of modern sleep

After the K-Pg extinction event, the environmental pressure to sleep during light time was softened and the current variety of mammalian chronotypes was possible, with high inter- and intra-specific variation of sleep in duration, timing, deepness, architecture, etc. (Elgar et al., 1990; Zepelin, 1994; Van Dongen et al., 2005; Tucker et al., 2007; Tang et al., 2007; Gander et al., 2010; Grant & Van Dongen, 2013; Dillon et al., 2015). Nevertheless, the diurnal rest, i.e. sleep, was certainly vital for the first mammals during millions of years but, after the K-Pc extinction, many mammals still managed to survive, despite showing widely different modes of sleeping, in every case adapted to the environmental variables. However, they maintained the essence, that is, the behavioral quiescence. This means that the importance of the newly developed variants of sleep was - and still is - minor. Indeed, sleep may be a paradigmatic example of an old, well-known principle of evolutionary biology: “the genetic and phenotypic variability is inversely related to the intensity of stabilizing selection” (Bulmer, 1971). As an example, the color variability of modern cars is infinite, but no car exists without wheels. Therefore, the relative importance of wheels vs color is indisputable. To apply this to sleep, we should search, among the phenotypic traits of sleep, those that always appear in the sleep of modern sleeping animals. Only after finding such trait(s) the evidence for its/their vital function in the entire mammalian class would be convincing.

To search such trait(s), we may remember that the main phenotypic traits of sleep are, 1) Behavioral quiescence, 2) Increased sensory thresholds, 3) Reversibility, 4) Specific sleeping sites, 5) Specific sleeping body positions, 6) Circadian regulation and 7) Homeostatic regulation (Piéron, 1913; Flanigan et al., 1973; Durie, 1981; Borbély, 1982; García-García, and Drucker-Colín, 1999). Noteworthy, six out of these seven traits can be easily observed also in resting wakeful animals. Indeed, waking animals may show quiescence, oscillations in sensory acuity, reversibility, specific resting places and bodily positions and, of course, circadian oscillations of rest-activity. Therefore, simple rest and behavioral sleep would be indistinguishable for a casual observer if it were not for the homeostatic regulation, whose primary function was, most likely, guaranteeing rest during day light time.

7. Discussion and conclusions

We recognize that the contents of the present review only deal with behavioral sleep. However, we would like to remark that sleep is a behavior and neither an electrographic pattern nor a set of biochemical reactions. Of course, the electrographic and biochemical patterns are essential for the processes underlying sleep, but they only are the hidden machinery allowing its behavioral expression (Vyazovskiy, 2015). Nobody would select an apple attending to its biochemical composition. When selecting an apple, we only look at color, size and organoleptic properties but nobody considers the biochemical components of the fruit. In the same vein, nobody would say that natural selection directly selected the electrographic signs of sleep or the neuronal and biochemical activities involved in the regulation of sleep. We are aware of the hypotheses proposing, for instance, that sleep serves for synaptic maintenance or for memory consolidation, among many others. However, to test these hypotheses, the researchers always compare the behavioral consequences of sleeping vs sleep deprivation (Vyazovskiy, 2015). In conclusion, the function of sleep should consist in guaranteeing the behavioral signs of sleep, among which, the quiescence is, probably, the most important one.

Nevertheless, the processes, hypotheses and facts described in the present review only hold for mammals. No NEB has been described in the evolution, from basal Archosauria to modern birds that have tetrachromatic vision and are basically diurnal – like their reptilian ancestors - (Husband & Shimizu, 2001; Matthen, 2007; Shimizu et al., 2009). Furtherly many birds make extensive use of UV light (Yokoyama et al., 2000; Cuthill et al., 2000), contrasting with the described protecting mechanisms developed by diurnal mammals to avoid UV exposure. Therefore, the similarity between mammalian and avian sleep must be the result of evolutionary convergence. Also, we know that sleep is currently considered to be universal in animals and has been well-characterized in invertebrates, for instance in drosophila flies, up to the point that many researchers believe that sleep is monophyletic. (see Bringmann, 2018, for instance). In contrast, the present report strongly suggests an evolutionary convergence for the mammalian and avian sleep that, for the time being, remains unexplained. Thus, we must conclude that, at least, sleep evolved three times: two in vertebrates – mammals and birds, separately, – and, in a third wave – much earlier - in invertebrates in which, only considering the immense phylogenetic distance between arthropods' orders (Emerson, & Schram, 1998; Edgecombe, 2010; Giribet & Edgecombe, 2019), the number of independent sleep phylogenetic lines might be much higher. It only remains analyzing if the function of sleep consists in guaranteeing rest also in non-mammals. However, after having reviewed the universality of rest, it remains as a plausible candidate, agreeing with several previous reports (Webb, 1974; Meddis, 1979; Nicolau et al., 2007; Siegel 2009, 2011).

The present review has presented some facts that never were considered when dealing with the evolution of sleep. The Nocturnal Evolutionary Bottleneck explains the set of physiological changes that determined the evolution of mammals from their reptilian ancestors. Then, we have proposed an after-consequence of the NEB, the sleep bottleneck, essential for the survival of nocturnal mammals. In addition, we remarked the importance of rest when confronted with the remainder traits of behavioral sleep. Under these premises, the single option available for early mammals was remaining immobile in light-proof burrows with closed eyes during light time. In other words, those pre-mammals capable of sleeping during light time survived, while the remaining ones were extinguished.

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