

REVIEW ARTICLE

Origin and Evolution of Sleep: Roles of Vision and Endothermy

J. LEE KAVANAU

University of California, Department of Biology, Los Angeles, California, 90095-1606, U.S.A.

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ABSTRACT: The origin of both sleep and memory appears to be closely associated with the evolution of mechanisms of enhancement and maintenance of synaptic efficacy. After the origin of activity-dependent synaptic plasticity, whereby single activations of synapses led to short-term efficacy enhancements, lengthy maintenance of the enhancements probably was achieved by repetitive activations (“dynamic stabilization”). These are thought to have occurred either in the course of frequent functional use, or to have been induced spontaneously within the brain to maintain synaptic efficacies in circuits that were in infrequent use. The latter repetitive activations are referred to as ‘non-utilitarian’ dynamic stabilization. With the evolution of increasing repertoires and complexities of behavioral and sensory capabilities—with vision usually being the vastly preeminent sense—brain complexity increased markedly. Accompanying the greater complexity, needs for storage and maintenance of hereditary and experiential information (memories) also increased greatly. It is suggested that these increases led to conflicts between sensory input processing during restful waking and concomitant ‘non-utilitarian’ dynamic stabilization of infrequently used memory circuits. The selective pressure for the origin of primitive sleep may have been a need to achieve greater depression of central processing of sensory inputs—largely complex visual information—than occurs during restful waking. The electrical activities of the brain during sleep (aside from those that subserve autonomic activities) may function largely to maintain sleep and to dynamically stabilize infrequently used circuitry encoding memories. Sleep may not have been the only evolutionary adaptation to conflicts between dynamic stabilization and sensory input processing. In some ectothermic vertebrates, sleep may have been postponed or rendered unnecessary by a more readily effected means of resolution of the conflicts, namely, extensive retinal processing of visual information during restful waking. By this means, processing of visual information in central regions of the brain may have been maintained at a sufficiently low level to allow adequate concomitant dynamic stabilization. As endothermy evolved, the skeletal muscle hypotonia of primitive sleep may have become insufficient to prevent sleep-disrupting skeletal muscle contractions during ‘non-utilitarian’ dynamic stabilization of motor circuitry at the accompanying higher body temperatures and metabolic rates. Selection against such disruption during dynamic stabilization of motor circuitry may have led

to the inhibition of skeletal muscle tone during a portion of primitive sleep, the portion designated as “rapid-eye-movement sleep.” Many marine mammals that are active almost continuously engage only in unihemispheric non-rapid-eye-movement sleep. They apparently do not require rapid-eye-movement sleep and accompanying ‘non-utilitarian’ dynamic stabilization of motor circuitry because this circuitry is in virtually continuous use. Studies of hibernation by arctic ground squirrels suggest that each hour of sleep stabilizes brain synapses for as long as four hours. Copyright © 1997 Elsevier Science Inc.

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INTRODUCTION

Roffwarg et al. [170] conjectured that spontaneous, repetitive activations of circuitry in the central nervous system (CNS) during rapid-eye-movement (REM) sleep in the human embryo facilitate circuit development and maintenance. They suggested that such activations during REM sleep maintain circuitry throughout life. This concept has been highly fruitful, with further contributions and elaborations by many investigators, and with increasing experimental support.

The concept provided the basis for a paradigm of “dynamic stabilization” (DS) of neural circuitry [reviewed in 103] (Circuits storing inherited information—frequently referred to as “hard-wired,” e.g., circuits for autonomic functions—are referred to as “phylogenetic memories,” while those storing experiential information—such as learned responses—are referred to as “ontogenetic memories.”). According to the paradigm of DS, synaptic efficacy in circuits storing ontogenetic and phylogenetic memories is enhanced, and the enhancements are maintained lengthily, by frequent functional use, and by activations induced by spontaneous oscillatory brain activity. Since the spontaneous activations maintain enhanced synaptic efficacy, but

Address correspondence to: J. Lee Kavanau, University of California, Department of Biology, Los Angeles, California, U.S.A., 90095-1606, U.S.A. Phone, (310) 825-3474; Fax, (310) 206-3987

usually do not trigger circuit functions (often inhibited by temporarily increased activation thresholds), they are referred to as being 'non-utilitarian.' In the following, unless functional DS is referred to specifically, 'non-utilitarian' DS is implied.

Pursuing the logical implications and consequences of a long-term maintenance of synaptic efficacy by DS has led to the formulation of a chain of causal evolutionary neural links, from the development of activity-dependent plasticity of synapses in simple metazoans to the neural adaptations represented by REM sleep in mammals and birds [104]. The present paper explores: (a) the implications of the dominating influences of visual input on brain activity, the evolution of parcellation of the processing of visual input between the retina and central brain regions, and the existence of unihemispheric sleep in birds and cetaceans, for the origin of primitive sleep; and (b) the role of endothermy in the bifurcation of sleep into non-REM (NREM) and REM states.

It has long been suspected that self-generated, spontaneous brain oscillations play a fundamental role in brain activity [117]. The primary function of many of these oscillations during sleep may be the DS of synapses in infrequently used circuitry. Examples of spontaneous oscillatory activity that may accomplish DS are: the theta rhythm of REM sleep, which may enhance synaptic efficacy in the hippocampus [103,153,154,171]; irregular sharp spikes of NREM sleep, which may potentiate synaptic efficacy in targets of the hippocampus [21,28]; and continuous synaptic bombardment from the intrinsic cortical networks that generate the slow sleep rhythm of NREM sleep, which may reinforce synapses in cortical association neurons [201,207].

Spontaneous brain oscillations also may maintain memories over the short term. In the proposal of Lisman and Idiart [116], they would provide timing signals that control serial processing of multiple short-term memories in neural networks, each memory stored in a different high-frequency (~ 40 Hertz) nested sub-cycle of a network's low-frequency oscillations. Firing of network neurons could be sustained by a neuromodulator-induced transient increase in membrane excitability (short-term activity-dependent efficacy enhancement) that is refreshed on each cycle of network oscillations (dynamically stabilized).

Oscillating and resonating neurons and networks are able to project their rhythms and generate synchronous firing in large neuronal populations [117]. Neurons in neocortical layer 5, in particular, can generate highly synchronous activity and impose it on other neurons in the cortex [31]. Discharges can be synchronized on a millisecond time scale even when the neurons are widely distributed [192]. Reinforcing activations of DS apparently have their origin in these oscillations. Oscillatory neurons are widely distributed, being found in the neocortex, entorhinal cortex, thalamus, hypothalamus, inferior olivary nucleus, olfactory system, and brain stem. The major part of thalamocortical connectivity is devoted to self-generated oscillatory activity (largely reentrant [45] or reverberating) that produces global oscillatory brain states [118].

One source of selective pressure for the evolutionary origin of neurons with oscillatory firing capacities, or for their development from 'primitive' non-spiking oscillator or pacemaker cells, may have been the need for spontaneous activations to enhance the efficacy of synapses in infrequently used circuits. In support of this conjecture, single neurons with endogenous oscillatory properties, with multiple conductances contributing to their rhythmic bursts, and with capacities for modulated switching between a variety of activity patterns, are of wide taxonomic occurrence [52,64,205].

Oscillator neurons and pacemakers occur even in organisms with the simplest nervous systems, for example, sea anemones and corals [196]. That a need for self-generated neural activa-

tions probably is of very ancient origin is suggested by the finding that "coordinated spontaneous activity. . . is a fundamental feature of the most primitive nervous systems" [18]. One expects the primordial basis for long-term memory to exist in some 'simple' nervous systems, and this coordinated spontaneous activity appears to be the underlying mechanism.

NEURAL ACTIVITY IN SLEEPING AND WAKING BRAINS

Before embarking on considerations of the selective pressures for the evolution of primitive sleep and the NREM and REM sleep states, it is desirable to review briefly some aspects of the ontogeny of sleep. Because DS appears to be associated with spontaneous, endogenous brain waves, it also is desirable to review briefly the origins and properties of some of the principal waves.

Ontogeny of Sleep States

Perhaps the most convincing evidence for a role of DS in the enhancement and maintenance of synaptic efficacy is the requirement for spontaneous, stereotyped activations of synaptic terminals, synapses, and neural pathways in the embryo and fetus to achieve the development, maturation, fine-tuning, and maintenance of circuits [26,73,83,125,140,170]. Synapses must transmit frequently and axons must conduct impulses to achieve full development and maintenance. Lacking frequent spontaneous activation, axonal terminal bulbs cannot mature and initiate synapse formation; nor can neuromuscular junctions and innervated muscles mature [83,95]. Activations also are essential in subsequent synaptic remodelling through selective eliminations [162], as are activations by specific inputs at specific later times for normal sensory and related cortical development [147]. Indeed, under the influence of excess activations, cortical connections that normally would be eliminated during development are retained [60].

Almost all synaptic activations in embryonic circuitry in some animals occur during sleep states. The ontogeny of sleep in humans is illustrative. The waking state does not appear in fetuses until the 37th week of gestation, a mere two weeks before birth [80]. Most sleep from weeks 28 to 30 until birth is in the REM state [29,167,233]. Since this is a period of rapid neurogenesis, spontaneous endogenous circuit activations during the last 7 to 9 prenatal weeks occur largely during REM sleep. The situation is extreme in fetal sheep, in which there is no waking state; all fetal movements appear to represent phasic events during REM sleep [168].

Non-rapid-eye-movement sleep does not become significant until the 34th to 36th week of gestation, accounting for 36–50% of sleep by the time of birth and becoming increasingly dominant during the next 8 months. In some altricial ('helpless' at birth) species, NREM sleep appears only weeks after birth; many muscular twitches characterize the REM sleep of members of these species during the first postnatal weeks [90].

The human neonate sleeps for 16–17 h per day, after which sleep time gradually decreases with age. At 8 months of age, only 33% of total sleep (13–14 h) is in the REM state. The value declines to 20–25% in the adult and to less than 15% in late adulthood [11,183]. Continuing large amounts of sleep and extensive self-activations of circuitry in the infant and child are accompanied by intense new learning (with a concentration on motor learning) and highly active growth, synaptogenesis, cerebral development, and organization of the CNS [65,83,163]. Emergence and subsequent synchronous development of perception, action, and reasoning also occur during these periods [195].

Considering these circumstances, in conjunction with a large body of evidence for processing of information by the brain during sleep [see 103,104], one is led to the strong presumption that DS largely supports the establishment and maintenance of phylogenetic and ontogenetic memory circuits in the infant and child during sleep states. Circuit consolidation and maintenance appear to be accomplished by the same means in the adult [73,170,201].

Some Electroencephalographic Correlates

Beta and alpha rhythms in humans. Rhythmic activity in the adult neocortex, as revealed by electroencephalograms (EEGs), is pervasive. With a commonality of waveform over extended areas, EEGs represent potential differences arising from extracellular currents generated by synchronized, rhythmic de- and hyperpolarizations of billions of synaptically coupled thalamocortical neurons [54,156]. In highly aroused and attentive waking states, EEGs consist of low-amplitude fast waves (14–30 Hz), the beta rhythm or “activated” pattern [148]. Fast, spontaneous, synchronous activity in the beta/gamma range (20–40 Hz), including activity specifically at 40 Hz, also occurs in thalamocortical networks (over the entire cortical mantle) during waking (and REM sleep) [118,119,200]. Except in extreme anesthesia or severe hypothermia (see HIBERNATION AND DEEP TORPOR), absence of an EEG reflects death of the brain [157].

In a quiet room, at rest, on eyelid closure, the beta rhythm gives way to long trains of predominantly high amplitude, synchronized slow waves (8–13 Hz)—the alpha rhythm. This rhythm originates in the primary visual area of the parietal-occipital cortex (striate cortex) and is blocked by sudden sensory stimuli or mental activity [14,117,120,182,234]. Blocking by sudden sensory stimuli can occur even in unconscious patients with brain-stem generated alpha coma [157].

Alpha rhythms characteristically wax and wane in amplitude and become slower with age [111,212]. As stage 1 of NREM sleep approaches, they disappear [55]. A prominent alpha rhythm during putative sleep is a presumptive indication of arousal [110]. Alpha activity increases during early stages of certain states of meditation, which have been compared to states of sleep or relaxation [17,86].

EEG changes on eyelid closure in other vertebrates. Phenomena closely related to the alpha rhythm occur in most mammals and birds [24,55,97,120,176]. During restful waking, with the eyelids open or partly closed, increases in slow-wave EEG activity occur. Such synchronous slow-wave EEG activity appearing in the restful waking pigeon (*Columba livia*), domestic hen (*Gallus domesticus*), and domestic livestock (pigs, horses, sheep, cows) increases on closing the eyelids [152,176,217].

Comparable EEG activity in reptiles (and some amphibians and fishes) is high-voltage, arrhythmic spiking that emerges during quiescence and sleep. This is related, and similar in waveform, to mammalian ventral hippocampal spikes—which are rare or absent in active waking, augmented in restful waking, and increase still further during NREM sleep [24,66,67,210]. As examples, in crocodylians (*Caiman sclerops* and *C. latirostris*), incidence of such spiking increases upon eyelid closure [51]. Similar, less marked, EEG changes occur in iguanas (*Ctenosaura pectinata* and *Iguana iguana*). Conversely, spiking is reduced or eliminated on eyelid opening by sleeping iguanas or arousal of sleeping tortoises (*Geochelone carbonaria*) and chameleons (*Camelot jacksoni* and *C. melleri*) [24,50,210]. (These changes involving opening or closing of eyelids with alterations in the amount of high-voltage, arrhythmic, EEG spiking, contrast with those at higher frequencies exhibited on arousal from restful wak-

ing, usually by novel or environmental stimuli. In some fishes, amphibia, and reptiles, the presentation of such stimuli evokes increases in the amplitude and apparent synchrony of high-frequency EEG waveforms [112].)

Non-rapid-eye-movement sleep in humans. In progression from NREM stages 1 to 4, vigilance declines monotonically but non-linearly [47,156] and the energy metabolism of the brain decreases progressively [124]. The responsiveness of temperature sensor neurons in the preoptic hypothalamus declines to a lower level than during waking [75]. The major synchronized EEG waves of stages 2 to 4 are spindle oscillations, delta waves, and the slow sleep oscillation [201,207]. Spindles, signalling stage 2 (about 45–50% of sleep time) and announcing loss of consciousness, are waxing and waning synchronized waves at 7 to 14 Hz grouped in sequences that recur each 3 to 10 s. They are generated in reticular thalamic networks and impose their rhythm on target thalamocortical neurons [121,198].

As a NREM sleep bout progresses, spindles become reduced and progressively overwhelmed by lower frequency (1–4 Hz), high voltage, thalamocortical delta waves. The latter, comprising stages 3 and 4, also known as slow-wave sleep, account for 13–23% of sleep time [29,87,199,208]. The neocortical slow sleep oscillation (<1 Hz) appears to play a pivotal role in integrating or grouping spindles and delta waves [201,207]. Only its self-limited duration and its interruptibility by exogenous stimuli distinguish normal stage 4 sleep from coma [157].

Avian unihemispheric non-rapid-eye-movement sleep. The occurrence of unihemispheric sleep in birds, in which the optic nerves decussate (cross over in the optic chiasm) virtually completely or completely in most adults [150,211], is highly relevant. Sleep with the lids of one eye open has been observed in 29 avian species in 13 orders, including greatly diverse representatives. A NREM-like (“quiet sleep-like”) EEG state—during which DS presumably is taking place at a high level—occurs in the brain hemisphere contralateral to the closed eyelids; a wakeful EEG occurs ipsilaterally.

Both right and left unihemispheric sleep occur in each individual—manifested overtly by slow-paced or periodic opening and closing of eyelids or “peeking;” lids of both eyes remain closed during brief periods (measured in seconds) of REM sleep [4,13]. When birds sleeping with the lids of both eyes closed open the lids of only one eye, opening is accompanied by a wakeful EEG on the contralateral side (e.g., in the telencephalon of chicks, *Gallus domesticus*) [152]. Avian sleep is so closely associated with eyelid closure that it is asserted that the eyelids “close only in sleep” [96], and that “blinking” in some species is a good behavioral index of sleep [4,24].

Rapid-eye-movement sleep in humans. A marked increase in the excitability of the brain’s internal communication systems occurs during REM sleep [74,130]. The level of energy metabolism is similar to or slightly greater than during waking [124]. As the process of substituting behavioral control of body temperature for neuronal mechanisms continues, the responsiveness of preoptic hypothalamic temperature sensor neurons reaches its lowest level [75]. All forebrain and cerebellar neuronal groups, with the possible exception of the amygdala, receive strong tonic and phasic excitatory influences [203]. The accompanying EEG rhythms are remarkably complex and lack low-frequency components [29,73,170].

Synaptic excitability in thalamic and cortical regions appears to surpass waking values [193,202,204]. Rapid-eye-movement sleep arousal thresholds are quite variable and, at their maxima, are exceeded only by those for stage 4 NREM sleep [25,77,106,118]. Frequent, usually unremembered, transitory

arousals during REM sleep (microawakenings) often terminate a dream and sometimes initiate lucid dreaming [107,110].

Ponto-geniculo-occipital spikes. Markedly increased internally generated signals, the ponto-geniculo-occipital (PGO) waves or spikes during REM sleep are of wide taxonomic occurrence. They almost always appear a short time preceding the onset of REM sleep, but are not unknown at other times during NREM sleep, and also can be elicited during wakefulness. Absent or powerfully suppressed during waking in humans, they occur in response to external unexpected stimuli (as in the startle response) [74,77,123].

PGO spikes are the pacemaker for phasic events of brain activity in REM sleep, activating the sensory, emotional, mnemonic, and motor systems, with conveyance of specific signals to the forebrain [57,76,88,130,191]. Besides being a distinctive sign of dreaming, and heralding onset of rapid eye movements (REMs), PGO spikes are tightly coupled to and influence the movements, indicating a brain arousal state resembling alert wakefulness [130]. In several respects—time of occurrence, frequency increase within an REM period, and influences of REM sleep deprivation—the distribution and susceptibility of PGO spikes in other animals exhibit parallels with intense dreaming [109].

The theta rhythm and 'field irregular sharp spikes.' Two additional EEG components of significance in the present context are the 'theta rhythm' and 'field irregular sharp spikes' (SPWs). The theta rhythm plays an important role in waking infancy and childhood, and during restful waking and sleep in adults (the 4–7 Hz band) [14,148]. It is thought to facilitate the induction of LTP (long-term potentiation) in hippocampal circuits and to facilitate and control the flow of information to the hippocampus or through the hippocampus to targets [53,59,118,121,153,154,222,235].

Synaptic potentiation in targets of the hippocampus may be accomplished in conjunction with SPWs [22]. A concurrence between maximal SPW bursts, NREM sleep, and reduced hippocampal transmission thresholds provides persuasive support for the occurrence of information processing during NREM sleep [155,234,236] (information processing also is believed to occur extensively during REM sleep [104]). There are indications that SPW-associated population bursts in retrohippocampal neurons powerfully depolarize their postsynaptic neocortical targets, suggesting that population bursts represent a mechanism of hippocampal "replay" [28] (reviewed in [142]).

ORIGIN OF THE PRIMITIVE SLEEP STATE

As non-sleeping animals acquired increasingly complex brains, behavioral repertoires, and visual competencies, together with ever enlarging stores of ontogenetic and phylogenetic memories, increasing amounts of DS of memory circuits were required during periods of restful waking. Like sleep, restful waking (or inactivity other than sleep) in present-day vertebrates is not an exclusive function of external circadian rhythms, but is determined by additional internal regulatory mechanisms [214]. As employed in the following, "restful waking" (also sometimes referred to as "quiet wakefulness," "rest" or "drowsiness") is characterized minimally by behavioral quiescence (cessation of voluntary activity) unelevated sensory thresholds, characteristic postures, vigilance, and, at most, only brief and intermittent pupillary occlusion.

Eventually, with continued advances in brain complexity, a condition would have been attained in which greatly increased needs for DS of memory circuits led to significant conflicts with other circuit activities of restful waking. These circuit activities

would have involved chiefly the processing of sensory inputs, predominantly visual (see Interference with Information Processing).

The selective pressure for the evolutionary origin of primitive sleep may have been the need to achieve a more profound state of brain unresponsiveness to these sensory inputs during DS of circuitry than occurs during restful waking. If, under selective pressure, the brain were relieved of extensive needs to deal with environmental input (as it is during sleep), DS could have proceeded unimpededly. The resulting sleep would have been characterized overtly by behavioral quiescence, elevated sensory thresholds, rapid arousability, characteristic postures, and occluded pupils.

Sensory Input

Much of the brain of most mammals is involved directly in processing sensory information (preponderantly visual) and mediating motor performance [94]. Sensory input in waking mammals is modified at all levels of incoming pathways [159], encountering increasingly multifunctional neurons as it ascends from peripheral to central structures, particularly in the cortex [181]. For each sensory mode except olfaction, peripheral information ascends from the thalamus (the functional and morphological gate to the forebrain) to separate unimodal sensory neocortical systems; area 17 of the striate cortex is the primary receiving area for visual input of most mammals [69]. Of the several nuclei in the thalamus that are way-stations in pathways of visual input from the retina to the cortex, the dorsal lateral geniculate nucleus most directly subserves conscious, detailed focal vision. The ventral lateral geniculate nucleus is a prominent retinorecipient area in reptiles and birds [186] (see, also, *Retinal and Central Processing of Visual Input*).

Very short-term memory storage probably occurs in neocortical systems (for "... as long as the level of intervening interference is low" [43] or, in the Lisman and Idiart [116] proposal, for as long as systematic changes in the phase of network cell firing do not occur, as new information is added to the systems). The same systems probably also are final repositories for long-term memory, after hippocampal processing [43]. The basic processing modules of these cortical systems are the neuroanatomically complex cortical columns [143,205,234].

Through the influence of brainstem oscillators, thalamic neurons are key elements that gate the cycle of wakefulness and sleep states, and passage of synaptic information from areas of sensory perception to the cortex. The connectivity between the thalamus and cortex is bidirectional, with roughly an order of magnitude more corticothalamic than thalamocortical fibers. For example, pyramidal cells in layer 6 project back to the thalamic area where their input arises [117,118,205]. Frontal lobe output pathways control ascent from the thalamus, as they selectively inhibit relaying (by "dynamic filtering or gating" [184]) of irrelevant input [193]. Patients with frontal lobe dysfunction are unable to disregard such input [184], exhibiting widespread behavioral disorganization in which the normal structure of goal-directed behavior is disturbed [42,142].

The thalamus is in its optimal-transmitting or relay mode for sensory inputs (faithfully following them in terms of strength and timing) during active waking and REM sleep, when thalamocortical cells show an increased synaptic responsiveness and generation of tonic fast action potentials. It is in its rather stereotyped, rhythmic, burst-firing mode (~300–500 Hz) during restful waking and NREM sleep, when there is interference with the coherent (faithful) flow of sensory inputs to the cortical level. Burst firing results in the entrainment of cortical neurons and the

generation of oscillatory activity, such as the alpha rhythm, spindling oscillations, and delta waves [117–120]; all appear to be associated with DS.

Unimodal cortical areas relay information to their associated areas, and from them to their associated areas, etc., for further processing, sometimes with convergence of several modalities. Massive feedback pathways also exist, projecting from higher to lower cortical areas. Stimuli from the same event usually activate neurons in the same region. In these processes, the point-to-point topological mapping characteristic of almost all unimodal sensory regions usually becomes partially degraded [133].

Inputs from unimodal cortical areas, including a substantial visual component (conveying binocular information and directional sensitivity [38]), also converge monosynaptically (from layer 5, providing almost all of the output from the neocortex to the rest of the brain [31]), in various combinations, onto multi-sensory subcortical neurons in the superior colliculus. The latter is the homologue of the optic tectum in other vertebrates, where visual, auditory, and somatosensory signals converge (see *Nocturnal Predation and Decreased Retinal Processing*). Most of these neurons are efferents projecting via the crossed tectoreticulospinal system to brain stem and spinal cord loci involved in orienting movements of the eyes, ears, and head [197].

Cortical association areas also receive subcortical sensory inputs directly; the thalamic pulvinar nucleus projects to areas in the temporal lobe and to regions of adjacent parietal and occipital lobes of ‘higher’ primates [39]. Information from multimodal association areas converges directly or indirectly on the entorhinal cortex, where it receives its most refined analysis, as well as back to thalamic neurons [234]. Impaired retrieval of complex knowledge correlates with damage to the cortices located closest to the apices of feedforward chains culminating in the entorhinal cortex, and farthest from the beginning of feedforward chains in unimodal sensory cortices [34].

Each sensory system also sends inputs to separate parts of the amygdala [141]. Being massively interconnected with different unimodal and multimodal cortical sensory areas, this structure is in a position to receive highly processed cortical information and to mediate the association of memories formed through different senses [40]. On the output side, it is linked directly with motor, endocrine, and autonomic effector systems. It interprets incoming sensory information and integrates neuromodulatory influences on the storage and strengths of associated long-term memories, particularly those that are emotionally influenced [113,132]. It also may play an important role in the generation of 40-Hz EEG activity [118].

From the amygdala and entorhinal cortex information is relayed to the hippocampus [73,234]. Thus, if a single perceptual event is formed by the concurrent confluence of different sensory inputs, the highest order of perceptual abstraction of these inputs, together with emotional associations, are presented to the hippocampus for processing [118,234] (see [104] for a treatment of hippocampal circuitry).

Extensive lateral interactions within the hippocampus virtually wipe out any topological mapping from arrays of sensory receptors onto hippocampal coordinates [133]. Accordingly, by the time input has been processed by the diffuse elements of hippocampal circuitry, it is ‘supramodal’ [209]. From the hippocampus, information is relayed to other limbic structures and thence directly and indirectly to the neocortex. Recurrent feedback (or ‘replay’) from the hippocampus to the neocortex is thought to play a critical enabling role in gradually binding together sites storing different types of information in functionally specialized cortical processing areas [43,104,131], a process in

which response synchronization through corticocortical connections may play a major role [192].

Interference with Information Processing

An intrinsic basis for potential incompatibilities between the brain’s endogenous processing of information (whether involving DS, residual neural activity associated with prior input, or other functions) simultaneously with reception of sensory input, is that learning and memory involve many of the same cortical regions that process sensory information and control motor output [219]. Neuronal activity circulating in cortical and thalamic networks is known to be modified by activity engendered by incoming sensory information [223]. A classical example of sensory interference is alpha blocking by alerting stimuli [148] (other examples in [223]). Alternatively, processing of sensory input can be altered in different brain states. For example, fear conditioning of the brain leads to altered receptive fields for auditory processing [230].

As is well known, sensory input tends to act as a distraction to conscious mentation. Sensory input in one modality (even unattended) may alter or interfere with inputs in other modalities [112,197]. Also, relaying of higher order sensory information based on prior input from the amygdala and entorhinal cortex to the hippocampus during active waking, very likely is not fully compatible with simultaneous processing of ongoing sensory inputs. Several workers [23,108,126] have suggested that sensory input might interfere with endogenous information processing.

It should be emphasized that despite the potential incompatibilities referred to above, the continuous, dynamic interactions of sensory inputs with ongoing neural activities are intrinsic to waking brain function [14,40,111,219]. Even at its most basic levels, the CNS is not organized in such a manner as to yield particular responses for particular stimuli, but rather to accomplish particular objectives [62]. Rather than mirroring the external world, the CNS embodies a dialogue between the internal states generated by the intrinsic electrical activity of nerve cells and their connectivity, and the information reaching it from the senses [117]. Sensory stimuli gain their significance by virtue of triggering a preexisting disposition of the brain to be active in a particular way. If the stimulus is not put in the context of thalamocortical reality by becoming correlated temporally with the ongoing neural activity, it does not exist as a functionally meaningful event [119].

Selection Against Superfluous Visual Input During Restful Waking

The essence of waking brain function in the absence of volitional activity is the processing of sensory input, an enormous amount of which is required by vision [118], and a great deal of which is processed at a low level without visual attention [161]. Wide regions of cortex, including many cortical fields, apparently interact during even simple visual tasks [25]. Objects in the crowded visual environment compete for focal attention and behavioral action at many levels of the visual system, involving both automatic (pre-attentive) and cognitive (attentive) components.

Events leading to visual awareness involve substantial unconscious editing that de-emphasizes irrelevant information and adds interpretations and inferences about the meaning of the targeted information, modulated markedly by the viewers ongoing interests (‘state-dependent modulations’) and the behavioral significance of the stimuli [37,129].

Of over 52 cortical areas of the macaque monkey (*Macaca fascicularis*) neocortex, 25 functionally heterogeneous, ex-

tremely selective, hierarchically organized areas, representing simple to successively more complex stimuli and attributes, are devoted solely to visual processing. Another 7 areas also process visual information. The 32 areas together cover over half the surface of the brain [221]. A very rich subcortical network interconnects the cortical visual areas [237]. For example, each visual area in the owl monkey (*Aotus trivirgatus*) projects to approximately 5 to 15 sub-cortical structures and nuclei, many closely related to motor performance [92].

Similar conditions also apparently apply to the brains of tree shrews (*Tupaia glis*), bush babies (*Galago senegalensis*), and the domestic cat (*Felis domesticus*) [38]. Further, rhesus monkeys (*Macaca mulatta*) probably have at least 12 separable and differently specialized topographic maps of the visual field at the level of the visual cortex alone [238]. Mammals with much less neocortex and relatively small brains have only a few 'general purpose' visual areas [69,186] (see *Divergent Cortical Development in Mammals*).

Viewing this sometimes enormous visual requirement from the perspectives outlined above on sleep's primal function, and the potential for sensory input processing to interfere with ongoing neural activities, a strong selection against reception of superfluous visual input to central brain regions during inactivity would be expected. Retiring to dark or very dimly-lit quarters and remaining there throughout inactivity is one very straightforward response to such selection, though it would not always have been feasible or highly adaptive (see "... 'poor' sleeping surface dwellers" under *Implications for the Evolution of Sleep*).

Another response would be the evolution of mechanisms that greatly reduce or eliminate complex visual input to the eyes, correspondingly reducing or eliminating the need for central processing of visual information, and allowing the occurrence of less impeded or unimpeded DS and other endogenous neural activities. These circumstances draw attention to the ocular adnexa—principally eyelids—involved in reducing or eliminating the reception of visual information.

Ocular adnexa. The first vertebrates to invade land experienced an absence of moistening and cleansing actions on their eyes—previously provided by water—and unavoidable contacts of airborne abrasive particles with the cornea. The earliest adaptations to these terrestrial conditions apparently were fluid secreting structures internal to the eyeball, and two or more eyelids and new glands and muscles external to it [228]. Initially, the lids undoubtedly were transparent, for protection and enclosure only.

Other than some elasmobranchs, fishes lack eyelids and nictitating membranes. Only a few teleosts can alter the size of the pupil; other fishes occlude their pupils by rotating their eyeballs or with expansible opercula [228,229]. Nor do permanently aquatic amphibians or larval amphibians have eyelids. Only partial lids that have remained partially transparent have evolved in other amphibians. Frogs can retract the eyeball completely, or cover a partially retracted eye with the lower lid.

Lower eyelids usually are the major devices that effect occlusion of the pupils in birds and in reptiles that possess eyelids, but wide variations exist: in crocodylians, closure is effected by the upper lid; in some lizards, the eyelids are fused completely, forming a transparent spectacle (also present in snakes), in others they leave a small circular aperture; in still others a 'window' exists in the lower lid [218].

The lids usually are rendered entirely opaque by scales or feathers, or are partially diffusing (as in humans, pigeons, parrots, and songbirds [127]). Accordingly, their closure either excludes light completely or allows some diffuse transmission. Although very little is known about the evolution of ocular adnexa,

it seems likely that additional and improved mechanisms for moistening, lubricating, protecting, and maintaining the optical quality of the cornea (in which nictitating membranes participate) evolved as eyelids became opaque or diffusing.

The function of opaque or diffusing eyelids. The earliest reptiles (and amphibia) doubtless were diurnal, as are most fishes. (Three- or even 4-pigment color vision is possessed by some teleost fishes, amphibia and reptiles [210,228].) A large fraction of these vertebrates apparently have remained diurnal to the present day, although many species are secondarily diurnal [218,228]. Opaque or diffusing eyelids (for simplicity, referred to hereafter as "opaque eyelids") of most reptiles, whether presently diurnal or nocturnal, must originally have been adaptations for use in daylight and well-illuminated portions of twilight periods. Exclusion or diffusion of light would not have been adaptive during activity and would have served no purpose at night, at least in reptiles with diurnally-adapted eyes. Accordingly, the only needs for eyelid opacity could have been for protection from bright sunlight during basking or for occluding complex visual input.

The latter action is the most likely function of eyelid opacity. From the present perspectives, this translates to the virtual elimination of visual input to central visual areas of the brain, obviating possible interference with central information processing and DS of circuitry. Since the function of eyelid opacity is highly pertinent, the circumstance of the eyelids being predominantly open during basking, and not functioning for protection from sunlight, is documented in the following.

When the ambient temperature is low, many reptiles, particularly in temperate regions, spend a considerable part of the day basking motionless in direct sunlight (so-called heliotherms). There seems little doubt that the eyelids of basking small reptiles remain open most of the time, and that the eyes are variously employed. Predominantly open eyelids would be mandatory for sluggish, small reptiles warming up to the preferred body temperature early in the morning. In fact, 'approach distances,' maintenance of which requires constant visual vigilance, are greatest then [68]. Virtually constant vigilance for avian predators would be crucial.

The basking marine iguana (*Amblyrhynchus cristatus*) uses its eyes to orient relative to the sun [232], while the Jamaican anole (*Anolis lineatopus*) seems to maintain almost constant visual vigilance while basking, since it is most difficult to catch then [11]. Brief, periodic closure of the lids of one or both eyes while basking (and/or prior to "behavioral sleep") has been detected only in captive animals: iguanas (*Iguana iguana*) and Mexican lizards (*Ctenosaura pectinata*) [51].

Perhaps the most studied basking reptile is the tuatara (*Sphenodon punctatus*), which also is discussed in following sections. It is the most primitive and unspecialized living reptile—the only survivor in the order Rhynchocephalia—representing a primitive Permian reptilian grade. Despite living in a cold, temperate region, it is primarily nocturnal, but the visual system retains sufficient diurnal adaptations to enable 24-hour activity and acuity in bright light. The tuatara is an habitual basker during the activity season, and even emerges from so-called partial hibernation during the winter months to bask for hours on sunny days (with pupils in the slit condition). Basking animals apparently keep their eyelids open almost continuously, as they are very wary and retreat promptly to the nearby burrow on being approached [16,177].

To the limited extent that small reptiles close their eyelids during basking in temperate regions, the function of closure would appear to be to limit evaporative water loss [146]. In light of these considerations, it seems justified to conclude that the

opacity of reptilian eyelids functions primarily to eliminate complex visual information, rather than to protect the eyes from bright sunlight, which could be avoided readily by altering posture or orientation, basking in dappled shade, or averting the eyes.

Selection for pupillary occlusion. If, in addition to nocturnal inactivity, diurnal early reptiles also engaged in intermittent periods of daytime inactivity (“daytime napping”), as do many present-day vertebrates [24,97,102,194], a selective pressure would have arisen for opaque eyelids. This would have occurred as soon as brain complexity and visual proficiencies attained levels at which processing of visual input during daytime inactivity interfered significantly with DS of memories and other vital central neural processing.

As already noted, eyelid closure in many vertebrates, often even momentarily, is accompanied by increased slow-wave EEG activity or high-voltage, arrhythmic spiking, both presumably associated with DS. Accordingly, the first mechanism to evolve for facilitation of primitive sleep in conditions of illumination probably was exclusion of visual input by evolved opaque eyelids (or other occlusion of the pupils). For humans, eyelid closure obviates very extensive central processing of complex visual information and initiates the alpha rhythm, one of the presumptive effectors of DS. By this tactic, we achieve some of the benefits of sleep while awake.

Depression of Sensory Perception and Processing During Sleep

During much of sleep, perception of most sensory inputs (and their arousal value) is depressed, with the magnitude of the depression varying phasically in concert with PGO spikes [52,76,77,106]. Although the EEG reactivity to external stimuli is increased during NREM sleep [63], and the amplitude of most primary evoked cortical responses to sensory input during REM sleep is similar to or greater than in waking [118], one is not awakened by stimuli that would be perceived when awake.

With the thalamus and cortex engaged in synchronous oscillations, only a minor part of thalamocortical connectivity is devoted to the transfer of sensory input. Accordingly, the forebrain tends to become isolated from distracting environmental influences, with its activities confined largely to the functions of internally generated activations [73,89,114,118,159,205]. It is proposed that these functions include the consolidation of labile new ontogenetic memory circuits and the maintenance of stable existing memory circuits by DS. Accordingly, with extensive depression of sensory perception during much or most of sleep (including absence or exclusion of proprioceptive input during REM sleep [75]), circuit consolidation and reinforcing functions of the hippocampus and other information processing by the brain can proceed unimpededly.

The Organ That Most Benefits From Sleep

Many lines of evidence suggest that the CNS is the organ that most benefits from sleep [79]. Stated succinctly by Hobson [73], “sleep is of the brain, by the brain, and for the brain.” Indeed, the greater the complexity of encephalization of function of the mammalian brain, the greater its vulnerability to prolonged interruptions of normal sleep-wake mechanisms following fore-brain or rostral brain-stem injury [157]. The ability of some vertebrates to be active for long periods or continuously with, at most, unihemispheric sleep, is a strong indication that, for them, the brain either is the only organ to require sleep or that it requires no sleep.

The proposed origin and primal function of sleep would not rule out a subsequent or concomitant evolution of secondary ben-

efits. Indeed, for most vertebrates, such secondary functions of sleep as bodily rest and rejuvenation, regulation of hormonal secretions, and reinforcing of the immune system [48] also appear to come into play. The physiological and thermoregulatory continuities between sleep, shallow torpor, and hibernation in some mammals (see HIBERNATION AND DEEP TORPOR) and birds suggests that energy conservation also is a secondary benefit of sleep [15]. Additional functions might be accomplished by adaptive modulations of the activations of DS. The existence of multiple functions apparently confounds the results of studies of prolonged sleep deprivation seeking to identify sleep’s primary function [48].

The evolution of sleep in response to the proposed selective pressure is consistent with its apparent variability and discordant occurrence among ectothermic vertebrates [24,66,210] (see *Complex Retinal Processing and Non-Sleeping Vertebrates*). It should be noted that if DS is the major mechanism of consolidation and maintenance of neural circuits, as proposed, pathologies affecting its operation might have very diverse and debilitating consequences, among which could be the genesis of epileptiform activity.

Optic Nerve Decussation and Unihemispheric Sleep

Partial optic nerve decussation is believed to be plesiomorphic (the primitive ancestral condition) for vertebrates, with complete decussation having evolved secondarily in most birds, many fishes and reptiles, and some mammals [20,165,166,228]. For birds, initially pronounced retinotopic ipsilateral projections in the embryo undergo apoptotic elimination during ontogeny [150,211], leading to complete or nearly complete decussation in most adults. However, secondary recrossing fibers may exist at several levels of the brain, connecting the visual target areas of the two hemispheres [46]. For example, the telencephalic area of some diurnal and nocturnal raptorial birds, such as the burrowing owl (*Speotyto conicularia*) has a bilateral input, accomplished in geniculotelencephalic projections [101].

While the present analysis of the ultimate function and selective pressure for sleep raises the possibility that ectothermic ancestors of birds slept unihemispherically, it is more likely that unihemispheric sleep, and the complete decussation that makes it possible, are secondary adaptations for the aerial niche. The evolution of complete decussation would have been driven by at least two selective pressures: (1) to achieve unihemispheric sleep, which makes possible long, non-stop flights for hunting, and migratory flights of up to thousands of miles; and (2) to minimize or eliminate interhemispheric cross-talk in the interests of split-second decision making during rapid flight [102]. Selective pressures for other adaptations, such as independent scanning by the eyes ([228]; see, also, [8]), also might have played a role in the evolution of complete decussation in many non-mammalian vertebrates, including birds.

In view of known widespread unihemispheric sleep in birds, greater credence can be given to speculations that some birds sleep (unihemispherically) when migrating and when flying for months at sea. For example, the tern (*Sterna fuscata*) comes to land only when breeding, and easily becomes ‘waterlogged.’ According to Skutch, “. . . it sleeps, or at least takes whatever rest it needs in the air during months at sea” [see 7]. This also may hold for Swifts (*Apus apus*), which are widely reputed to ‘roost on the wing’ [see 134].

On long flights of migration and hunting (during which unihemispheric NREM sleep and DS of largely non-motor circuitry may occur), there presumably is very little need for DS of motor circuitry, as much of it would be in virtually continuous use or

in continuous use in the spinal cord and alternate brain hemispheres. Motor circuitry not in such use might undergo unihemispheric DS during periods of flight with NREM sleep, accompanied by “inconsequential phasic events,” including phasic modulations of ongoing motor activities (see [104] and *EVO-LUTION OF NREM AND REM SLEEP*).

Similarly rooted selective pressures for unihemispheric sleep probably led to the evolution of complete decussation in the ancestors of dolphins and some other marine mammals after radiation into the marine habitat. The condition of complete decussation in many fishes [165], including most adult teleosts [30], might have had a similar origin. One would most likely encounter unihemispheric sleep in fishes that are active unceasingly, including the ‘warm-blooded’ fishes and some cartilaginous species [24]. Indeed, Weber [229] suggests that a shark (*Galeorhinus canus*) sleeps while swimming.

Retinal and Central Processing of Visual Input

As concluded above, the selective pressure for primitive sleep in early vertebrates would have been the need to depress central processing of sensory input during periods of inactivity, so as not to interfere with DS and other endogenous brain activity. Since, as already noted, the very great preponderance of sensory input to be processed by the brains of most vertebrates is visual, the following treatment emphasizes mechanisms that have evolved in relation to visual input. This is not to denigrate the need to reduce or eliminate the perception and/or processing of other sensory inputs during sleep. But since, in general, other inputs probably interfere with DS of memories to a much lesser degree, they receive less attention in most of the following (but see *Mole Rats*).

Strategies to limit central processing. A priori, one can envision two major evolutionary strategies to limit central processing of visual input during inactivity. In one, evolution of opaque eyelids and closure of the lids of both eyes would have eliminated virtually all visual perception of the environment. In the other, eyelids could have been absent or remained transparent, with an increased role of retinal processing of information from the visual environment, and a lesser expansion of the role of central processing. Both paths may have been followed to varying degrees, depending largely on the anatomical and physiological substrates possessed, and upon the ecological and behavioral niches occupied. Implementation of the strategy of eliminating “virtually all visual perception of the environment” is discussed below in *Implications for the Evolution of Sleep*.

Complex retinal processing. The strategy of complex retinal processing of visual input, with a lesser emphasis on central processing, probably was available to almost all early vertebrates. It might well have been initiated, developed, and maintained to varying degrees in all, particularly as it might also have reduced response delays in prey capture and predator avoidance. At the very least, it would have reduced redundancy in the information transmitted centrally from the retina. The possible importance of complex retinal processing in this connection is suggested indirectly by the large size and heavy myelination of axons of the retinal fiber tract of the primitive accessory optic system and the basal optic root, itself.

These properties indicate a need to carry information rapidly to central targets from retinal cells engaged in a minimum of in situ processing. Into this category fall the peripherally located “displaced ganglion cells of Dogiel,” which mediate movements of the eyes in response to moving stimuli at the periphery and stabilize the eyes to the visual scene [99]. If peripheral-to-central transit times comprised a relatively insignificant portion of the

response delay, large, myelinated fibers would not have evolved in these locations. This suggests that it would have been highly advantageous to analyze critical visual information—say, evaluation of sources of potentially threatening movements—in the retina immediately upon receipt.

Depending upon the degree to which it relieved the brain of needs to process visual input centrally during inactivity, complex retinal processing in some early vertebrates might have lessened selective pressures for sleep, either eliminating a need for sleep or ‘buying time’ for animals for whom other adaptive modifications could not have evolved as rapidly as those of the retina. This strategy would have lost its effectiveness in postponing sleep, however, as brains became increasingly complex. In view of the great susceptibility of vertebrate eyes and the visual components of vertebrate brains to selective pressures accompanying altered behavioral and ecological influences (see below), the following circumstances are suggested.

The transition between restful waking and sleep in the course of evolution of early diurnal reptiles—the group of primary interest here (see *The ‘Bottleneck’ Theory and Divergent Pathways to Sleep*)—probably was gradual and may not have been irreversible. Exclusion of complex visual input from the retina may have become adaptive initially, adaptively neutral to maladaptive later, then adaptive again, etc., as animals shifted between secure and less secure—and variously illuminated—resting quarters, and between the employment of varying degrees of retinal and central processing of complex visual input. A need for sleep also would have been influenced by selective pressure for maintenance of accompanying secondary benefits. Selective pressures still may be operative in some vertebrates in establishing the balance between restful waking and sleep.

Of the ectothermic vertebrates studied with regard to engagement in, or absence of, sleep, four species already have been found for which complex retinal processing may have eliminated a need for primitive sleep. These are the bullfrog (*Rana catesbiana*), with occasional unilateral or bilateral closure of the eyelids, the sea turtle (*Caretta caretta*), with the condition of the eyelids unknown, the tortoise (*Testudo denticulata*), with the eyelids seemingly open or closed, and the American alligator (*Alligator mississippiensis*), with the eyelids rarely closed [refs. in 24]. In this connection, the retina of the leopard frog (*Rana pipiens*) is the most complex known in ectothermic vertebrates (see below).

Processing of visual information in mammals and non-mammalian vertebrates. Retinal processing occurs in all sighted vertebrates. However, varying degrees of increased specificity, integrative capacity, and structural complexity exist in the retinas of non-mammalian vertebrates, together with varying degrees of lesser capacity for visual processing in the rest of the brain (except in birds), as compared to most mammals (for a treatment of birds, see *Complex Retinal Processing and Central Visual Processing in Birds*).

In an extreme example of the non-mammalian-mammalian divergence, the retina of the leopard frog, with extensive serial synapses among amacrine cells and at least seven classes of ganglion cells, is much more complex, both anatomically and physiologically, than the retinas of primates, in which vision probably has been secondarily reemphasized [138,139]. Thus, the non-mammalian condition contrasts sharply with the relatively simple retinas and complex central visual processing in the brains of most mammals.

Four notable exceptions are a species of rats (*Rattus norvegicus*), one of rabbits (*Lepus cuniculus*) and one of ground squirrels (*Citellus mexicanus*), the domestic cat, and probably some related forms in which the degree of retinal processing

rivals that in the leopard frog. The ground squirrel has 15 morphologically distinct types of ganglion cells [85,138,231]. The rat may have as many as 8 million neurons (bipolar, amacrine, and ganglion cells) in its retina, as compared to only a fraction of that number in the lateral geniculate bodies (70,000 neurons) and the cortical visual centers (about 1.3 million neurons) [85].

The existence of such exceptions can be understood in terms of the great susceptibility of vertebrate eyes and the visual components of vertebrate brains to selective pressures accompanying altered behavioral or ecological influences [93,158,213,228]. “. . . diurnality and nocturnality come and go in evolution as mutatory capacity and ecological expedient direct” [228].

Mammalian-non-mammalian differences generally include an evolutionary trend toward increased prominence of mammalian retinogeniculate projections and striate cortex. Notwithstanding this trend, the retinotectal projections generally remain the major system. Probably more than 90% of retinal axons terminate within tectal layers in reptiles and birds, and the superior colliculus (mammalian homologue of the optic tectum) still receives the majority of retinal projections in most mammals (but only the smallest fibers). Primates are the major exception, in which retinogeniculate projections (to area VI in the occipital lobe) are dominant and retinotectal projections are markedly reduced [69,128,186,213]. In some birds, the retinogeniculate projection rivals or exceeds that of some mammals [99].

Since retinal ganglion cells are anatomically and functionally the most proximal neurons of the vertebrate retina—the conveyors of all visual information—their output must be influenced either directly or indirectly by all major types of neurons in the retina. The dominant direct influences appear to be exerted by bipolar and amacrine cells at their synapses with ganglion cells in the inner plexiform layer. These influences plus indirect influences of patterns of organization in the outer plexiform layer probably are the major factors that distinguish the retinas of different species [82,138].

The retinal ganglion cells of the mammalian retinogeniculate projection perform only a relatively simple analysis—“center surround” contrast and, in some cases, color. In non-mammals, ganglion cells have directionally selective receptor fields, more like the “simple” cortical cells of mammals [138,139,172] (see [138,172] for an exposition of ganglion cell response specificities).

In general, dendritic lamination of the inner plexiform layer, and a generally more complex organization of the horizontal cell population of retinas of non-mammalian vertebrates are indications that more complex analysis is carried out than in the retinas of mammals. The evolution of a great number of types of amacrine cells, containing an astonishing diversity and wealth of neurotransmitters and neuromodulators (the “amacrine explosion”), and their interactions with ganglion cells, are believed to underlie the diversity of visual analysis in the retinal ganglion cell population of non-mammalian vertebrates [213]. Every morphological type of amacrine and ganglion cell, as well as every type of photoreceptor, horizontal cell, and probably also bipolar cell, in the outer plexiform layer, appears to reflect distinct physiological properties [6,82,213].

Sophisticated visual analyses reflect a greater participation of central mechanisms in primates, and a greater participation of retinal mechanisms in frogs and rabbits. In the same vein, comparative studies support the view that complexity of ganglion cell form and function correlates inversely with degree of encephalization of visual analysis [173,213].

As Jerison [85] has remarked in connection with “. . . the elaborate organization of the [reptilian] retina . . . complex enough . . . to be considered as a true peripheral brain. . . it was

possible to encode distance information directly as events at different points or regions of the retina. . . visual systems of the brain itself, beyond the level of the retina, may have relatively little additional work to do.” And, “. . . it [the visual system] enables living frogs and lizards to strike at small (fly-sized) moving objects, but it does not enable these animals to distinguish between a fly and a black spot moved by an experimentalist. . . . In nature, however, it enables living reptiles and amphibians to capture their normal prey and, by analogous reflex mechanisms, to escape from predators by responding in appropriate ways to large moving objects.”

The ‘Bottleneck’ Theory and Divergent Pathways to Sleep

The ‘bottleneck’ theory. An evolutionary pathway for the non-mammalian-mammalian divergence of visual systems treated above is proposed in the ‘bottleneck’ theory [see 128,160]. This theory is of significance for the origin and/or evolution of sleep since it has implications not only for the non-mammalian-mammalian visual system divergence, but also for the evolution of other sensory systems and sensorimotor capabilities, all of which impact directly on complexity of brain composition and function and indirectly on requirements for restful waking and sleep.

In revised, up-to-date guise the theory proposes that diurnal, insectivorous forerunners of present-day mammals invaded nocturnal, terrestrial-arboreal niches during the Mesozoic era under the pressure of predation by the larger, diurnal, keen-sighted, dominant archosaurian reptiles, and facilitated by the tropical and subtropical climates of the times [85,102]. Invading mammalian forerunners diversified into several lineages during 140 or more million years of occupation of nocturnal niches (the various orders of eutherian mammals are believed to have diverged at about the same time from a common ancestor with a small forebrain and little neocortex). With audition and olfaction becoming highly developed, and visual systems becoming nocturnally adapted, the reptilian retinotectal vision became deemphasized, complex retinal processing became severely reduced, and forebrain cortical development began. Some unique mammalian ocular specializations originated as nocturnal adaptations of ‘bottlenecked’ Mesozoic ancestors [228].

Although some highly agile descendent mammals may have reentered diurnal and crepuscular niches earlier, the major reentrance by the descendent mammals is thought to have occurred near the end of the Cretaceous period, about 65 million years ago, as these niches became depauperated on extinction of the diurnal predatory archosaurs (the surviving crocodylians are largely nocturnal); other descendent mammals remained primarily nocturnal. In response to renewed selective pressures for diurnal vision in the contingent reentering diurnal niches, further evolution of their visual systems was characterized by greatly increased expansion into the neocortex and increased retinogeniculate connectivity—because of accompanying advantageous adaptations (see *New Visual and Visuomotor Competencies*)—rather than by increases in retinal processing and retinotectal connectivity.

Identity of the ‘bottlenecked’ animals. At the time nocturnal niches were entered, the invading animals already may have been of mammalian grade, such as members of the genus *Sinoconodon* or *Morganucodon*, in the Early Jurassic (about 205 million years ago). Alternatively, and more likely, the niches were entered much earlier, in the Middle Triassic (225–240 million years ago) by mammal-like reptilian ancestor of mammals. These might have been advanced cynodonts (eucynodonts), such as members of the genus *Probainognathus* or *Exaeretodon* [78,174].

Olfaction, temperature regulation, audition, and size. In the course of cynodont evolution, many characters became remark-

ably mammalian. Eucynodonts already possessed a good sense of olfaction and very likely were endotherms [71,78,105]. These adaptations would have greatly facilitated the invasion of nocturnal niches. Since sustained body temperatures would not be expected to have attained or approached those of living mammals, there would have been no need, initially, to parcellate sleep, if present, into NREM and REM portions—for DS of circuitry including largely non-motor components, as opposed to largely motor components, respectively (see EVOLUTION OF NREM AND REM SLEEP).

Presence of a tympanic membrane is yet to be established, but reduction in the size of the quadrate and postdentary bones, and loosening of their attachments, implies improved middle ear transduction sensitivity (to high frequencies). Such sensitivity in eucynodonts may not have fallen far short of that of living mammals [1,78]. But earliest mammals, themselves, did not yet possess a “mammalian middle ear”; quadrates still functioned as part of the mandible and postdentary elements as part of the suspensorium [1].

Most Mesozoic taxa relevant to mammalian phylogeny lie within the smallest order of vertebrate sizes [174]. Weights of most Mesozoic mammals are estimated at 20–40 g, in the shrew-to-rat range; giant forms were hardly larger than domestic cats [85,115].

Nocturnal niches and influences on sensory systems. Before the invasion of nocturnal, terrestrial-arboreal, Mesozoic niches by mammalian forerunners, the niches probably were empty of reptiles but rich in small invertebrates. They undoubtedly would have provided very favorable conditions for mammals or eucynodonts that could have overcome the demands made on their diurnally adapted sensory systems [85].

Selective pressures on the diurnally-adapted invaders would have operated to maximize predation success in dim and very dim light (contrast on the retina usually is more important than the absolute amount of light) and conditions of heavy overcast (i.e., near darkness). Strong selection for improved audition and olfaction would have contributed to enlargement of the brain—the midbrain for audition, and the forebrain for both audition and olfaction [85]. In this connection, when visual and auditory stimuli are present at low levels, bimodal localization is far superior to unimodal localization. An additional influence doubtless was the need for increased musculoskeletal coordination in terrestrial-arboreal habitats [32].

Balance of the bottlenecked predators’ eyes between acuity and sensitivity would have shifted heavily in favor of sensitivity (see below). Nonetheless, selection on central regions of the brain processing visual input could have operated within that constraint to maximize abilities to localize, recognize, stalk, and capture nearby small, elusive prey; the balance attained in the visual system very likely represented an optimizing compromise. With great retinal sensitivity albeit degraded acuity, and with 140 or more million years available for evolutionary “tinkering,” new and typically mammalian neural visual mechanisms contributing to maximizing these abilities could have evolved.

Thus, the need to adapt mechanisms of olfaction, audition, musculoskeletal coordination, and vision for existence and predation in conditions of dim and very dim light and heavy overcast probably were the major factors leading to initiation of forebrain reorganization in mammals, with the emergence of neocortex in the pallial mantle. These adaptations would have set the stage for the subsequent great post-bottleneck expansion of the new mammalian neural mechanisms during readaptation to diurnal niches and further exploitation of terrestrial-arboreal habitats.

Major reorganization of the skull, involving repackaging of a brain of ever increasing size was manifested throughout the his-

tory of eucynodonts, beginning in the Early Triassic [174], most of which probably was played out in nocturnal niches. Rowe [175; see, also, 49] suggests that, by the time of the first true mammals, the neocortical size increase had nearly doubled brain volume. But the cortex at that time probably was mainly sensory and sensorimotor [91,92].

Concerning the principal initial influences on the eye, itself, on entering nocturnal niches, sustained selection on a diurnally-adapted eye results in: (a) increased slenderness and numbers of receptor cells in the retina—with corresponding increases in retinal sensitivity, reductions in visual acuity, and loss of color vision; (b) development of tapeta (leading to increased sensitivity and visual acuity); and (c) non-uniform enlargement of components of the eye (producing brighter retinal images) [228]. Two other influences on the retina and central brain regions proposed by the bottleneck theory may be accounted for as follows.

Nocturnal predation and decreased retinal processing. As the bottlenecked animals were the hunters, prey capture in dim and very dim light would have been facilitated very little, if at all, by reduction of response delays through complex retinal processing. At a distance, small invertebrate prey (and small lizards in the Cretaceous) would have been detected, recognized, approached, and roughly localized, using audition and olfaction.

In this connection, the laminated superior colliculus of many present-day mammals has a visuotopic map in its superficial layers and topographically aligned somatosensory and auditory maps in its deeper layers. Inputs from different modalities interact and even compete for neuronal control (see *Mole Rats*). Instruction and feedback across modalities probably can aid in the development of an ordered map in one modality if the map for another modality already is developed. Indeed, great advantage accrues from interactions between visual and auditory spatial information because these sensory modalities offer different and complementary information for the localization of stimuli, and interact in a cooperative manner. Visual and auditory maps remain aligned in alert behaving animals, even though vision and audition provide information in different coordinate frames [224]. The homologous reptilian structure, the optic tectum, is primarily responsible for visually guided reactions toward prey, including approach, orientation, and capture, that sometimes may involve the whole body [10]. Regarding olfaction, of all the major subdivisions of vertebrate brains, the olfactory forebrain has expanded the most in terrestrial mammals [39], an elaboration that doubtless evolved during the exceedingly lengthy nocturnal Mesozoic sojourn of mammalian ancestors.

Once within sight during starlit and moonlit nights, albeit with much reduced acuity, prey would have been stalked quadrupedally and captured using head and jaw-grasping movements [see 102]. Prey capture in conditions of heavy overcast probably also would have been feasible, even by olfaction alone. For example, in some salamanders the olfactory system seems to operate with precision in detecting, identifying, and localizing prey in total darkness. The Italian lungless salamander, *Hydromantes italicus*, localizes a nearby prey animal so precisely that it can snap its tongue directly toward it [172] (see, also, below). On nights of heavy overcast, particularly, the diet probably was supplemented with seeds and nuts [149] (supported by dentition studies [105]; very few fruits were present before Cretaceous times [see 102]).

Nor is it likely that avoidance of predation would have been facilitated by reduced response delays in Mesozoic nocturnal niches, because of the probable absence of larger, nocturnally-adapted, terrestrial-arboreal predators. Without a need to minimize response delays, complex retinal processing, doubtless possessed by virtually all early vertebrates, would have lost one aspect of its apparent adaptive value. Upon the evolution of

opaque eyelids, the other aspect also would have been lost. Deemphasis of retinal processing would have resulted in strong selective pressures for extension of visual processing into the reptilian dorsal ventricular ridge and/or dorsal cortex, and for their great expansion and assumption of new mammalian capabilities in either or both regions.

The feasibility of predation by small terrestrial vertebrates in dim and very dim light, heretofore not fully appreciated, is shown by studies of tuatara and salamander predation. The retina of the tuatara is dominated by secondarily modified cones (termed "polysynaptic secondary rods" or "low-threshold cones" by Underwood [218]). The eyes are set in large orbits, partially retractable, possess upper and lower opaque lids and nictitating membranes, as well as tapeta and well-developed Harderian glands. As noted earlier, the nocturnally-adapted visual system retains sufficient diurnal adaptations (including slit pupils) to enable 24-hour activity [35,36,169].

The tuatara has only mediocre olfaction and audition (low frequencies only, with the least specialized inner ear of any reptile), neither sense being very useful in prey capture. It hunts both on the ground and in trees. Of all reptiles, the locomotion of the tuatara, though quick and brisk when hunting, is most primitive, sharing many features with urodeles [36]. Captive tuataras approach and seize 7-mm-long beetles (*Chaerodes trachyscelides*), cocking the head toward, and grasping, them with a darting movement and lightning-like snap of their powerful jaws. This occurs at illuminance levels as low as 0.0062 lux ($\sim 1/50$ th full moon). It is suggested that tuataras also can hunt by starlight [137].

Even more impressive results have been obtained with nocturnal salamanders (which lack audition). Italian lungless salamanders can detect, approach, and capture odorless moving prey models at illuminance levels of only 0.001 lux ($\sim 1/300$ full moon). Fire salamanders, *Salamandra salamandra*, can orient the body toward (for which the optic tectum is essential), approach, and snap at odorless moving prey models at levels as low as 3×10^{-7} to 3×10^{-6} lux (but not at 3×10^{-8} lux), ranging roughly from starlight obscured by clouds to unobstructed starlight [172].

New visual and visuomotor competencies. Even after eyes became well adapted to dim and very dim light, there would have been an exceedingly lengthy continued selection on other visual system components for improved localization, recognition, tracking, and capture of nearby prey. The largely cortical visual and visuomotor mechanisms of mammals have come to provide new kinds of competencies for such activities beyond the abilities of complex retinal processing and the largely midbrain control by ectothermic vertebrates [81]. These superior competencies, alone, might account for increased emphasis on central visual processing in mammals, independently of lessening utility of complex retinal processing in nocturnal niches.

Thus, there is no evidence that fishes or amphibians (some having projectile tongues) attacking moving prey can 'lead' them by anticipating trajectories, as can mammals, an ability that depends on visual cortex. Additionally, frontal cortex appears to play a key role in 'spatial planning,' and visual cortex appears to be important for detecting relative motion, and advantageous for shape recognition [81]. Amphibians, most snakes, lizards, many carnivorous turtles, and the tuatara either do not recognize, or usually disregard, stationary visual prey, a limitation that also may apply to carnivorous mammals whose prey seek to avoid detection by 'freezing' [137,172,228]. (For salamanders, a visually perceived lack of motion inhibits the snapping response. The effect is reduced by prey odor and disappears in

the absence of light, whereupon the response is elicited by olfaction alone [172].)

These new visual and visuomotor competencies would have been highly advantageous to a nocturnal terrestrial or terrestrial-arboreal predator feeding primarily on small invertebrates. With many tens of millions of years in nocturnal niches available for ultra-fine tuning of faculties, even very moderate selection might have produced significant cortical accommodations. Though doubtless falling far short of the cortical processing that occurs in bright light, accommodations for dim light, nonetheless, probably entail extensive central processing of visual input.

Divergent cortical development in mammals. The above proposal is consistent with the finding that many placental mammals, that apparently remained primarily nocturnal at the end of the Cretaceous period, possess typical mammalian cortical features. Exceptions to this generalization occur among the nocturnal insectivores—usually considered to have the most primitive features among living placental mammals. For example, the neocortex of the European hedgehog (*Erinaceus europaeus*), though multilayered, comprises only a cap on the rest of the forebrain, with a quite small striated area (where the afferent fibers of the visual radiation terminate). Though not excellent, hedgehog vision is better than that of most terrestrial shrews [91,158].

Some presently nocturnal forms probably passed through post-Mesozoic periods with differing emphases on crepuscularity, arboreality, and fossoriality than possessed at present (some few vertebrates appear to be almost solely crepuscular, such as, the salamanders, *Triturus vulgaris* and *T. alpestris* [72]). The persisting reptilian organization of the eyes of monotremes (egg-laying mammals), however, seems a consequence of long-standing strong nocturnality [228]. And monotremes are well in advance of marsupials and insectivores in relative brain size and brain differentiation [85].

The body of evidence provided by monotremes, marsupials, and insectivores, taken in conjunction with the retention of complex retinal processing in some placental mammals, support the following view. Divergent mammalian neocortices may have arisen through independent expansion and differentiation to facilitate diverse visual and behavioral adaptations by some early lineages in different nocturnal adaptive zones during, as well as after, Mesozoic times.

Such diverse adaptations might have been brought about by differing amounts of encroachment into, or retreat from, crepuscular, arboreal, and fossorial niches. With nocturnal niche occupation lasting for tens of millions of years, in both the Mesozoic and Cenozoic, it seems quite likely that changes of topography, climate, flora, and fauna engendered such differential encroachments or retreats in different lineages.

Implications for the evolution of sleep. Once diurnal early reptiles approached the threshold of a need for primitive sleep, that is, a need during inactivity for great reduction or elimination of central processing of complex visual input, various paths toward attaining it could have been followed. No anatomical adaptation to facilitate sleep would have been necessary in reptiles active throughout the day, retiring to very dimly lit or dark quarters when lower limits of their visual capabilities were reached during dusk, and resuming activity when they were exceeded during dawn. With virtual absence of visual input at night (for diurnally-adapted eyes), transparent eyelids would have sufficed for protection and fluid retention. Unimpeded DS during sleep would have consolidated and maintained memory circuitry.

Another category of such diurnal reptiles includes those that engaged in intermittent periods of restful waking during the day in safe, but illuminated, retreats. The evolution of opaque eyelids and their closure during daytime rest would have facilitated prim-

itive sleep, although the employment of complex retinal processing might have delayed its acquisition. The great flexibility conferred by being able to obtain briefly the benefits of sleep at any time during the day and, consequently, require less lengthy and deep uninterrupted periods of sleep during the night, would have been highly adaptive, and appears to be possessed by many vertebrates. Thus, many so-called poor sleeping surface dwellers rely heavily on vigilance and the capacity for flight for safety during inactivity periods [210]. For example, sleeping, captive reptiles possessing opaque eyelids characteristically open those of one or both eyes for brief periods, without a change of posture [50]. Much these same considerations would apply to arrhythmic vertebrates with primarily nocturnal visual adaptations but with retention of a fair degree of visual acuity in daylight.

Complex retinal processing probably existed in the ancestors of eucynodonts or early mammals long before they entered nocturnal niches in Mesozoic times. They also may already have acquired primitive sleep. Any bottlenecked animals that were only on the threshold of acquiring primitive sleep, that utilized safe daytime resting quarters, but were not entirely shielded from daylight, probably also would have followed the first strategy, that is, acquiring primitive sleep during inactivity via sustained closure of evolved opaque eyelids.

Reentry into diurnal niches by descendent mammals that had acquired sleep and no longer employed complex retinal processing would have been accompanied by profuse adaptive radiations of their visual systems. Advances in visual proficiency by further perfection of processing in a multiregional visual cortex could have been realized relatively readily, since conflicts between DS and sensory processing would have been obviated by primitive sleep.

Some non-sleepers with transparent eyelids might have been included in the contingent reentering diurnal niches. For them, any arising conflicts between DS and central processing of complex visual inputs during intermittent daytime periods of restful waking would have provided ever augmented selection (particularly with increasing brain complexity) for opaque eyelids and primitive sleep. Such daytime periods of restful waking would have been strongly promoted during the transition from primarily nighttime to primarily daytime activity.

In the event that some of these non-sleepers with transparent eyelids were included in the contingent that remained nocturnal, increased selection for opaque eyelids and primitive sleep would have followed any encroachments into crepuscular niches (which would have been favored in some animals as Cenozoic climates became more temperate), together with other refinements of the visual system and increased central processing. “. . . the real danger is that [pure-rod species] will see too much light . . . if

photomechanical changes, pupil mobility, or lid apparatus is unable to reduce the stimulation of . . . rods to a comfortable value” [228]. Even if remaining nocturnal, changes of behavior or habitats in this latter contingent, of a nature that led to exposure to light during inactivity, also would have favored the evolution of opaque eyelids and primitive sleep.

Complex Retinal Processing and Central Visual Processing in Birds

Some reptiles, perhaps including the ancestors of birds, may have acquired sleep relatively gradually, buying time for the transition through the strategy of complex retinal processing. The accompanying lesser response delays in predator avoidance and prey capture would have supplemented the primitive mechanism for rapid responses to peripheral stimuli provided by the accessory optic system and nuclei [70,99]. Because of the possession of this latter mechanism, movement perception does not decrease with eccentricity within the retina [69]. In this connection, the fast-acting, vigorous, visual accommodating mechanisms of birds differ from those of reptiles in only minor respects, whereas none of these mechanisms has survived in any mammal [228].

Some smaller Mesozoic archosaurs—the forerunners of birds—invaded the greatly expanding, relatively safe arboreal niches, in which they evolved endothermy and flight.¹ In the course of this evolution, the avian retinotectal visual system inherited from reptiles became enormously elaborated, with the result that birds possess a highly proficient, essentially “super-reptilian” visual system [128]. Together with many ectothermic vertebrates, they possess retinopetal projections [186] (see [102] for a consideration of selective pressures for the evolution of avian flight and a treatment of the avian visual system).

Whereas mammals could dispense with complex retinal processing, it remained indispensable in the visually highly proficient, fast moving birds, with brains specialized for high-speed decision making [102]. In them, there would have been a strong selection for both reduced response delays and increased response speeds, that is, for complex retinal processing, rapid neural transmission, and the highest tolerable, sustained body temperatures, which even have come to approach lethal limits [see 102].

Reflecting the complexity of retinal processing, the number of morphological types of ganglion cells in avian retinas apparently exceeds that known in any other vertebrate except the ground squirrel and domestic cat (see above), numbering at least eight in the domestic chick retina [136]. Likewise, only birds, in which precision and elaboration of retinal layers reaches its peak, exceed lizards in the laminar purity and thickness of their inner

¹ It was proposed that the following factors favored retention of ectothermy and flightlessness in arboreal lizards, as opposed to those promoting selection for endothermy and flight in avian ancestors. “The ancestors of lizards deviated from a path leading toward flight and endothermy because they never passed through a surface-nesting stage. This omission probably traced to the fact that they derive from a later reptilian lineage. The latter, perhaps, achieved the practice of shallow egg burial under somewhat less equable climatic conditions or slightly different reproductive habits. The different conditions or habits probably conferred lesser advantages to surface nesting and greater advantages to alternate ovarian function and multiple clutching in shallow [-ly buried] nests, with incubatory periods of about twice those common in birds (6–7 weeks in Green Anoles). (There did, however, exist early, relatively small, insectivorous Eolacertilians and even gliders, but these have left no trace of scales modified to confer more favorable aerodynamic properties.)

“Accordingly, with no obligatory need to shade, shield, and guard eggs in exposed surface nests, the ancestors of anoles also would have experienced no selective pressure for increased insulation from solar rays nor for advanced metabolic mechanisms for achieving homeothermy. In consequence, they would not have evolved insulative, featherlike modifications of scales nor achieved primitive metabolic stages in the development of endothermy. Downward climbing, thin bodies with long, fragile appendages, and foot-pad development were favored, rather than insulative scales with aerodynamically favorable properties for tree-to-ground jumping, such as for quick access to threatened surface nests.

“Furthermore, having arrived much later on the scene than the corresponding avian ancestors (perhaps the late Cretaceous period, although one Triassic genus, Paliguana, with debatable lacertilian affinities, is known from Africa), they probably would have found diurnal flying insects no longer as abundant, unexploited, or readily accessible as in the Jurassic period, so that selection for tree-to-ground jumping as a hunting tactic for catching large flying insects in flight would have been weakened or non-existent” [102].

nuclear and ganglion cell layers [228]. The avian retina “. . . is the most beautiful and elaborate in its architecture in the animal kingdom; layers and sublayers are clearly defined with each cell accurately in place” [41].

The mechanisms of visual information processing in the brains of birds are thought to be fundamentally different from, but at least as efficient as, those in the mammalian striate cortex [186]. Although neuronal circuits in the avian telencephalon are virtually identical to those found in mammalian neocortex, they differ in their final patterns of alignment. Rather than being disposed in juxtaposed laminae, they are more commonly found as groups of interconnected nuclei [100]. Only the wulst regio hyperstriatica, whose anterior portion is considered to be the avian equivalent of the somatosensory-motor cortex of mammals, has a laminar configuration [186]. However, even though largely non-laminated, the avian telencephalon can mediate visual performances of a complexity rivaling and even exceeding those of mammals, previously thought to have been correlated uniquely with cortical lamination [see 102].

Some ectotherms also have evolved along the pathway of body temperatures increased beyond the ambient level during activity, increasing speed of responses and further facilitating predator avoidance and prey capture. Thus, ‘warm-blooded’ fishes and insects, animals that possess some degree of thermoregulatory ability, can maintain body temperatures well above that of the environment during activity [210].

EVOLUTION OF NREM AND REM SLEEP

Most lines of evidence suggest that NREM sleep is, or most resembles, the primitive sleep state [66,89,134,239]. Sleeping ectotherms, such as reptiles, do not engage in REM sleep [29,66], which exists only in birds and mammals. REM sleep correlates with a highly developed forebrain in both groups, reflecting highly developed dorsal and dorsolateral ventricular ridges in birds, and a highly developed cortex in mammals [73,89,100].

Both NREM and REM sleep exist in all studied marsupial and terrestrial placental mammals [2,29,135,239]. Mammalian and avian sleep are very similar in most respects, but, except in hatchlings, REM sleep usually accounts for only 2–10% of total avian sleep time. It occurs in much briefer episodes, measured only in seconds [5,29,135], longer during the night than during twilights [97].

REM Sleep Atonia and the Activation of Motor Circuitry

During NREM sleep in mammals, skeletal muscle tone merely is reduced—by partial release from the sustained firing of motoneurons that maintains it during waking [27]. During REM sleep, on the other hand, muscle tone is absent and monosynaptic and polysynaptic spinal reflex activity are minimal or absent [75,106]. Lack of muscle tone traces ultimately to active motor inhibition by reticular neurons in pontine centers of the peri-locus coeruleus region. These project to a bulbar reticular zone which, in turn, projects to the spinal cord, causing hyperpolarization of alpha motoneurons, greatly increasing arousal thresholds [122,154,188,206]. REM sleep atonia is interrupted briefly by excitatory inputs that produce REMs and other characteristic muscle-driven phasic events (see 104). Most significantly for the function of REM sleep, associated brain-stem phenomena intrinsically involve activation of cortical and subcortical motor areas during this sleep state [130,206].

Since the cortex is incapable of making a motor response without marginal departure from REM sleep [9], the few outbursts of gross movement tend to occur at the beginning or end

of REM sleep bouts. Correlating with the muscle atonia, REM sleep is a protective state for generalized seizure events [187]; a grand mal epileptic seizure never occurs during REM sleep, nor does REM sleep ever occur immediately after a seizure [12]. Though commands for motor activity are very frequent in dreams, dream movements tend to be intermittent and to involve muscles whose contractions are of too little consequence to disturb sleep.

Bifurcation of the Primitive Sleep State into NREM and REM Sleep

Influence of Endothermy and High Metabolic Rate. It is suggested that all ontogenetic and phylogenetic memory circuits not in frequent use undergo DS during the primitive sleep state of present-day ectothermic vertebrates. The reduction in skeletal muscle tone that occurs during primitive sleep apparently suffices to prevent sleep-disruptive movements during reinforcement of synapses in motor circuits. But as early mammals engaging in primitive sleep evolved progressively increasing sustained body temperatures and metabolic rates, a condition probably was approached at which mere reduction in muscle tone no longer sufficed to prevent sleep-disruptive movements during DS of motor circuits.

Accordingly, evolution of more powerful mechanisms for inhibiting muscle contractions would have been favored. In the absence of such mechanisms, skeletal muscle contractions during DS of motor circuitry would have severely disrupted sleep, as they do in the essentially equivalent pathological ‘REM sleep behavior disorder’ [122]. In this disorder, dreamed and executed motor activities—kicking, shouting, jumping out of bed, and fumbling for hallucinated objects—closely parallel one another [122,178,180,185].

These circumstances apparently led to the adaptive modification of a portion of the primitive sleep state. Whereas skeletal muscle tone probably was merely depressed in primitive sleep, it was abolished in the course of partial evolutionary conversion to REM sleep, in which there is even a degree of depression of sympathetic muscle tone [164]. (Sleep in the echidna, *Tachyglossus aculeatus*, a primitive egg-laying mammal lacking REM sleep, may represent the closest approximation to the primitive mammalian condition [3,89,190] { when body temperatures and metabolic rates would have been lower }. Moreover, using rates and variability of brain-stem neuronal discharges as criteria, echidna sleep shares properties of both NREM sleep { lower rates compared to waking } and REM sleep { increased rate variability compared to waking } of other mammals [190]. In this connection, the echidna and other monotremes possess almost ‘entirely reptilian’ eyes; but for the presence of ‘ciliary webs,’ their retinas, and those of marsupials, might easily be mistaken for those of nocturnal reptiles [228].)

By means of this modification of primitive sleep, DS of infrequently used pathways containing motor components would have become associated largely with REM sleep, and DS of infrequently used pathways containing largely non-motor components with NREM sleep. This interpretation accords with the findings of Siegel and coworkers, which suggest that NREM sleep is not primitive; both NREM and REM sleep probably evolved in parallel from primitive sleep [189,190]. Karmanova and Lazarev [98] had previously adopted a similar view, namely, that both REM and NREM sleep have been developing concurrently. (To regard NREM sleep as the primitive sleep state gives primacy to the presence of a degree of muscle hypotonia, but does not take into account the composition of circuitry undergoing DS.)

A need to minimize disruptive movements probably would have applied with even greater force during fetal development, when REM sleep vastly predominates. The development and maturation of circuits during this period require a high level of DS (see *Ontogeny of Sleep States*). Thus, it would have been important to minimize full-blown contractions of skeletal muscles (as opposed to mere tremors, twitches, and occasional turning and limb extensions), as they probably would have interfered significantly with developmental processes.

These relations between endothermy, REM sleep, and non-utilitarian DS of motor circuitry receive support from observations in hibernating mammals (see HIBERNATION AND DEEP TORPOR) and birds. They engage in REM sleep during activity seasons, but spend less time or none in REM sleep in states of reduced or minimal body temperatures and metabolism, which are entered from NREM sleep [15,33,135,226]. Such findings in relation to influences of temperature on REM sleep are most reliable, as each animal acts as its own control. On the other hand, conclusions about the function(s) and relationships of REM sleep based upon comparisons between different species are rendered suspect by the often confounding influences of species-specific differences. For example, efforts to find close correlations across birds and mammals between REM sleep and variables such as total sleep time, degree of immaturity at birth, or safety of sleep sites, have been largely unfruitful [189].

Absence of REM sleep in continuously active marine mammals. From the present perspectives, marine mammals that swim almost continuously [24,144,145,151,215] require no REM sleep because their motor circuitry undergoes virtually unremitting functional DS, that is, it is reinforced through lengthy, almost continuous use. Dolphins engage almost exclusively in unihemispheric NREM sleep (e.g., <2% bihemispheric NREM sleep in *Tursiops truncatus* [see 24]), a condition in which their brain hemispheres alternately (every 1 to 3h) are in this sleep state. Stereotypic swimming in circles usually occurs during sleep but there also may be "quiet hanging behavior." (The relatively small amount of REM sleep in most birds, many being active continuously during the day [24], could owe to at least two circumstances. First, there may be a routine daily use of more of their motor circuitry than occurs in most mammals [103,104]. Second, some aspects of flight and walking movements are not coordinated in the brain but in the highly developed avian cervicothoracic and lumbosacral spinal intumescentia [see 102]. This is most relevant because intrinsic oscillatory neuronal activity in the spinal cord is at the foundation of locomotion [61,118]. In effect, comparatively less motor circuitry in the brains of birds needs reinforcing during sleep.)

Dolphins, whales, and probably some other marine mammals without binocular vision are exceptional among mammals; their optic nerves decussate completely [166,227]. This also is true of many fishes, Crocodylia, the tuatara, and some lizards, snakes, and turtles [165]. As in birds, dolphins that sleep unihemispherically often have the lids of one eye open (the "sentinel" eye) [144]. Other inverse correlations between amount of REM sleep and activities forming, maintaining, or employing motor circuitry also are known [103].

SLEEP IN INVERTEBRATES, ECTOTHERMIC VERTEBRATES, AND MOLE RATS

Criteria

In view of these considerations, emphasizing the roles of perception of the environment and processing of visual input, it can be suggested that the most reliable criteria for distinguishing sleep from restful waking in ectothermic vertebrates are elevated

thresholds for sensory stimuli, occlusion of the pupillary apertures, behavioral quiescence, characteristic postures, and rapid arousability. The presence of muscular hypotony would be indicative but not necessarily determinate, as it also might occur during restful waking (for example, neck muscle tone is absent whenever echidnas are not actively moving [190], suggesting that DS of infrequently used motor circuitry occurs during both restful waking and sleep). For the same reason, inconsequential phasic events would not be diagnostic, and their occurrence could be influenced significantly by temperature. While the presence of an EEG would be essential and is a valuable guide, EEG properties might vary considerably, being influenced largely by the degree of brain complexity. For example, the slow-wave activity characteristic of mammals and birds is not to be expected from the brains of fishes, amphibians, or reptiles, as it requires a well-developed neocortex (or ventricular ridges) [66,88,210]. Some degree of alterations of EEGs with state of vigilance would be expected but might be subtle, or inutile to differentiate transitions between different states. Other investigators [24,51] have cautioned against too great a reliance on EEG data.

Invertebrates

As noted above, the honey bee sleeps, and other invertebrates with complex eyes, including, at least, many arthropods and cephalopods, also probably sleep, depending upon behavioral and visual proficiencies and brain complexity. Behavioral sleep, including behavioral quiescence with species-specific stereotypic postures and elevated arousal thresholds, have been observed in bees, wasps, flies, dragonflies, grasshoppers, butterflies, moths, and a scorpion (*Heterometrus longimanus*); enforced behavioral wakefulness in a cockroach (*Leucophaea maderae*) and a scorpion (*H. spinnifer*) was followed by compensatory rebound in behavioral quiescence [24].

Non-Sleeping Vertebrates

Most ectothermic vertebrates probably engage in primitive sleep. Apparent exceptions, presumably facilitated by complex retinal processing, include the previously mentioned bullfrog, sea turtle, tortoise, and alligator, and any unceasingly active fishes that should be found not to engage in unihemispheric sleep. Other possible exceptions among fishes—that would be dependent upon an absence of complex visual input—are those for which vision plays a negligible or no role. Many fishes can survive on food procured non-visually, and many arctic species are deprived entirely of vision by overlying ice blanketed perpetually with snow [228].

It is not surprising that a bullfrog, two chelonians (turtles and tortoises) and a crocodylian (and perhaps some close relatives) do not sleep. Evidence for sleep among vertebrates is least conclusive among amphibians, whose brains still are at a generalized level, with their evolution being even more conservative than those of fishes. Thus, the reticular nuclear groupings, such as raphe groups and the locus coeruleus, present in cyclostomes, plagiostomes, teleosts, and ganoids generally are not present in amphibian brains [210,228]. Crocodylians are archosaurs and skeletally, at least, are very little changed from their Triassic ancestors. Chelonians are the most primitive living sauropsids (reptiles and birds). Though the lineage has undergone extensive structural evolution and bifurcated into pleurodires and crypto-dires (a division based on the manner of bending the neck on retracting the head into the shell), among all living vertebrates chelonians probably most aptly deserve the designation "living fossils" [85].

The Tuatara

Many characteristics of the tuatara make it a most interesting subject for the study of its states of inactivity. Indications of the primitiveness of its brain are the possession of a pineal-parietal eye, lack of a neopallium (a relatively small layer of cells on the anterior roof of the cerebral hemispheres in most reptiles), a cerebellum only slightly more developed than in many amphibians, and a resemblance to amphibians and some fishes in the origin and distribution of its cranial nerves [36,169].

Among reptiles, its nocturnal activity occurs at the lowest body temperature (6.2–16°C) and lowest metabolism, and it has the longest incubatory period. It has a slower growth rate than any lizard, great longevity (sexually mature at about 20 years), and complete optic nerve decussation [35] (allowing independent optical scanning). Though tuatara literature is voluminous, there has been no mention of sleep. The only information bearing even remotely on this topic are reports of “partial hibernation” during winter months, “. . . it spends most of its time motionless” [16], “. . . tuataras may emerge from their burrows at any time of the day or night in the forest . . .” [177], and “. . . at all times when not in view they [captive animals] were considered to be sheltering inside a burrow” [58].

Sightless Cave Dwellers

Assuming that reduction or elimination of sensory input—primarily complex visual information—to reduce interference with DS of brain memory circuits, is the primal function of sleep and the basis for its origin, how has loss of sight impacted on congenitally sightless cave-dwelling vertebrates?

No mention of sleep exists in a fairly extensive literature on sightless animals inhabiting caves. For vertebrates, the adult eye is described as having sunk beneath layers of connective and lipid tissues or as having migrated toward the brain and become “buried” in the orbit. The vagal lobes and forebrain, however, are enlarged, associated with the importance of chemoreception [160,172,220,225,228]. Periods of activity and rest of cavernicoles typically alternate throughout 24 h periods [220]. The degree of degeneration of the eyes of some salamanders and fishes seems to vary with length of isolation [44,160]. Unless salamanders are disturbed, they appear to be resting at all times or moving very slowly [44].

Mole Rats

Visual mechanisms of mole rats (*Spalacidae* and *Bathyergidae*) have largely regressed and atrophied (including size reduction of visual centers in the brain [33]). The animals are exquisitely sensitive to non-visual sensory input; for audition this can be attributed to the possession of an auditory input to the dorsal lateral geniculate nucleus and to cortical regions that correspond to visual areas in sighted rodents [224]. The attained stage of regression of the visual system of subterranean mammals cannot be correlated with phylogenetic age of the species nor its relative restriction to, or participation in, the subterranean mode of life [19]. Complete disappearance of the eyes has not occurred in any mammal [41]. Two reports of sleep exist—in the species, *Heterocephalus glaber* and *Spalax leucodon* [84,134].

Three possible bases for the persistence of sleep in mole rats can be suggested. Waking central processing of non-visual sensory input, for example, auditory input in the dorsal lateral geniculate nucleus and visual cortical areas, may interfere excessively with DS; secondary benefits of sleep may have become so great as to be indispensable; or the elapsed time since radiation into fossorial niches may be too short for sleep loss to evolve by neutral selection.

This latter alternative seems unlikely because the oldest fossils of mole rats date back to the Lower Miocene [179]. On the other hand, both of the first two alternatives may play roles.

HIBERNATION AND DEEP TORPOR

We noted earlier that an absence of EEG activity reflects death of the brain, except when it is under the influence of extreme anesthesia or severe hypothermia [157]. The state of deep torpor of the Arctic ground squirrel (*Spermophilus parryii*) involves severe hypothermia, with an absence of EEG activity for many days. Since, from the present perspectives, EEG components play roles in the DS of memories, parameters of hibernation and torpor for this animal have the potential to provide unique data. These would relate to the capacity of nerve cells to maintain synaptic efficacies in the absence of brain waves, and to the amount of time that synaptic efficacies can be maintained after DS accompanying given amounts of NREM and REM sleep. The following examples are based largely on findings of Daan et al. [33].

The body temperature of the euthermic Arctic ground squirrel lies in the range 36–38°C. During hibernation (generally entered from NREM sleep) squirrels cycle periodically between euthermia and a state of deep torpor at –2 to 5°C, the latter occurring in bouts lasting 1–3 weeks. Thus, at –2 to 5°C, when the metabolic rate is roughly 1/8th to 1/16th that in euthermia (assuming a Q_{10} of 2), synapses retain their functional capacity for as long as 3 weeks in the seeming total absence of DS.

In ground squirrels that hibernate at higher temperatures, for example, at brain temperatures above 9–10°C but less than 25°C, such as the golden-mantled ground squirrel (*Spermophilus lateralis*), brain electrical activity arises from thalamic neurons firing mostly at rates that correspond to their typical euthermic rates during NREM sleep. In shallow hibernation at brain temperatures greater than 25°C, these squirrels spend about 80% of the time in NREM sleep [216].

At the ends of the 1–3-week bouts of torpor of the Arctic ground squirrel, warming of the body occurs spontaneously for 4–6 h, accompanied by a “virtually zero amplitude EEG” and a high amplitude electromyogram associated with shivering thermogenesis. This warming phase, which occurs in all hibernators, arouses the animals to states of euthermia, which are maintained for an average of roughly 18 h. The first 12 h of each euthermic period are spent mainly cycling between NREM and REM sleep. Waking occurs primarily during the last 6 h of arousals, with the squirrels remaining in a curled hibernating posture. Times spent in the three vigilance states average 53% in NREM sleep, 14% in REM sleep, and 33% in waking.

Assuming that the need to restore enhanced synaptic efficacies through DS is the basis for periodic returns to euthermic sleep states during the long (5–6 months) hibernating season, about 16 h ($12 + 6 \times 2/3$) of DS during euthermic sleep suffice to enhance synaptic efficacies in the CNS of the Arctic ground squirrel for 1–3 subsequent weeks at –2 to 5°C. Roughly extrapolating 1–3 weeks of deep torpor to time under euthermic conditions (assuming a $Q_{10} = 2$), the period of synaptic efficacy maintenance would be roughly 0.7 to 4 h for each hour of sleep. (This extrapolation accounts only for temperature-dependent alterations in normally occurring breakdown of molecules essential for synaptic function [see 103,104]. Activity-dependent breakdown of these molecules also would come into play in euthermic states, and periods of efficacy maintenance would tend to be shortened.)

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