The Sleep Neuroscience Primer: Student Edition

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Sleep Neurology

- What physiological changes accompany sleep?
- How does the brain sleep?
- Why does the human brain sleep?
- Does it sleep differently from the brains of other animals?
- What happens when the human brain is sleep deprived?

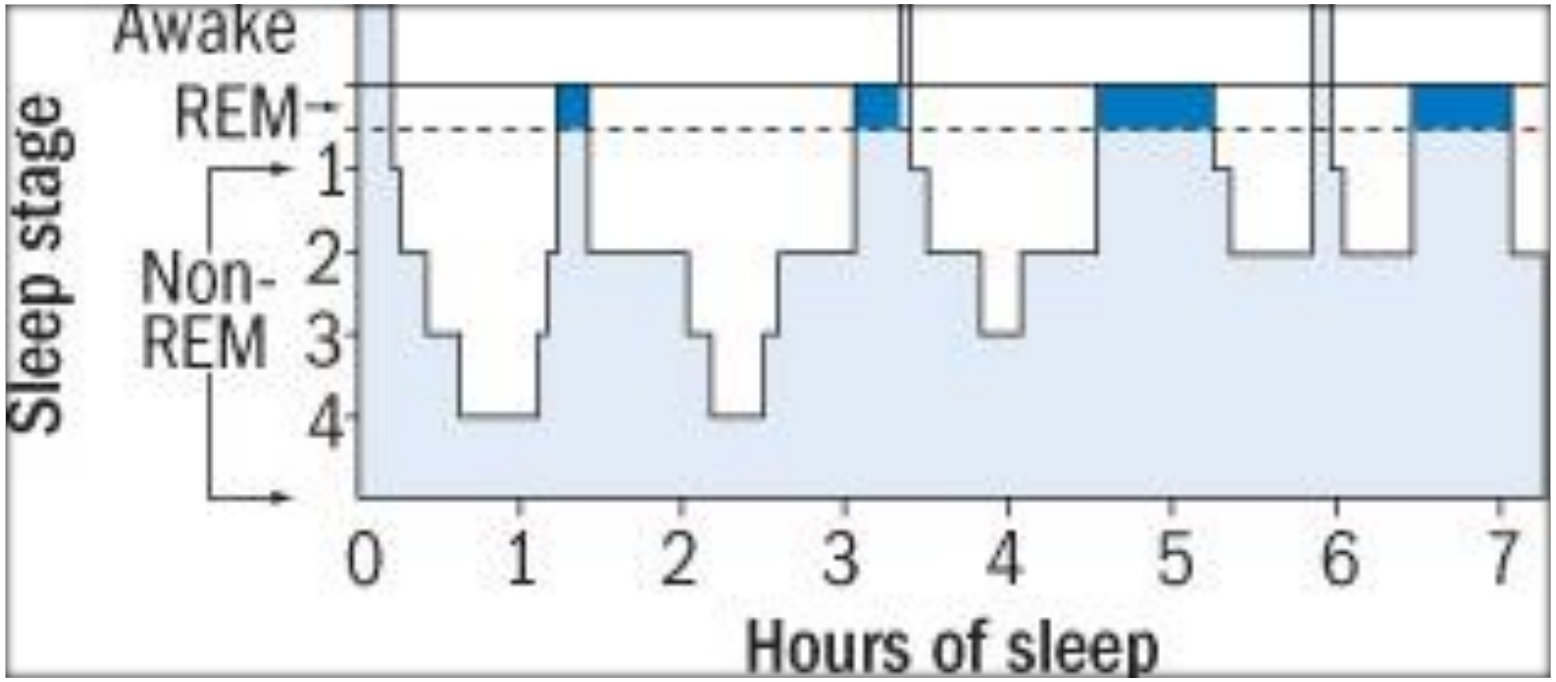
Sleep Architecture

- Sleep architecture is a term used to describe the division of sleep among the different sleep stages using specific EEG, EOG, and chin EMG criteria. It also involves the relationship of the individual sleep stages to each other .
- Sleep can be differentiated into NREM sleep and REM sleep. NREM sleep can be further subdivided into stages 1, 2, 3, and 4 sleep.
- NREM stages 3 and 4 sleep are often collectively referred to as slow wave or delta wave sleep.

Definition of Sleep

- Stages of sleep:
  - Stage N1 is drowsiness
  - Stage N2 is a bit deeper
  - Slow wave (Stage N3) or deep sleep is harder to wake-up from
  - REM is when most of your dreaming occurs

Normal Sleep Hypnogram



More REM as sleep continues

General information

- NREM and REM occur in alternating cycles, each lasting approximately 90-100 minutes, with a total of 4-5 cycles.
- In the healthy young adult, NREM sleep accounts for 75-90% of sleep time (3-5% stage I, 50-60% stage II, and 10-20% stages III and IV). REM sleep accounts for 10-25% of sleep time.
- Total sleep time in the healthy young adult approximates 6-8 hours.
- The newborn sleeps approximately 16-20 hours per day; these numbers decline to a mean of 10 hours during childhood.
- In the full-term newborn, sleep cycles last approximately 60 minutes (50% NREM, 50% REM, alternating through a 3-4 h inter-feeding period).

General information

- Pregnancy:
  - 1st trimester (increase in total sleep time, daytime sleepiness and nocturnal awakening)
  - 2nd trimester (normal sleep)
  - 3rd trimester (increased nocturnal awakening with subsequent daytime sleepiness and decreased total sleep time)
- In the elderly: SWS decreases and N2 compensatory increases, increase in latency to fall asleep and the number and duration of overnight arousal periods, time in bed increase with subsequent complaint of insomnia.
-

Brain Plasticity, Sleep and Aging

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In humans, aging is often associated with a decrease in total sleep duration, an increase in the time it takes to fall asleep and, most significantly, a decrease in sleep efficiency [39]. In other words, the percentage of time in bed spent asleep decreases progressively with age, from more than 90–95% in adolescents to less than 80% in 70-year-old subjects. Sleep composition also changes, with a relative increase in superficial sleep stages (stages N1 and N2) and a decrease in deeper stages rich in slow waves (N3, slow-wave sleep [39]). In fact, one of the most prominent sleep changes associated with aging is the decrease in slow-wave activity (SWA), which is already obvious in middle age [40, 41]. SWA, defined as the EEG power between 0.5 and 4 Hz during non-rapid eye movement sleep, is a convenient and quantitative way of measuring the number and amplitude of non-rapid eye movement sleep slow waves. More crucially, SWA is the best established marker of sleep need and sleep intensity, because it peaks at sleep onset and decreases with the time spent asleep. Moreover, staying awake from approximately 3 to approximately 24 h results in progressively higher SWA levels at sleep onset, and naps during the day reduce SWA the following night.

TYPE OF SLEEP	% Sleep For Infant	% Sleep For Young Child	% Sleep For Young Adult	% Sleep For Elderly Adult
Stage 1	< 5 %	< 5 %	< 5 %	8 -15%
Stage 2	25-30%	40-45%	45-55%	70-80%
Slow Wave Sleep	20%	25-30%	13-23%	0-5%
REM Sleep	50%	25-30%	20-25%	20%

MISSING LINK

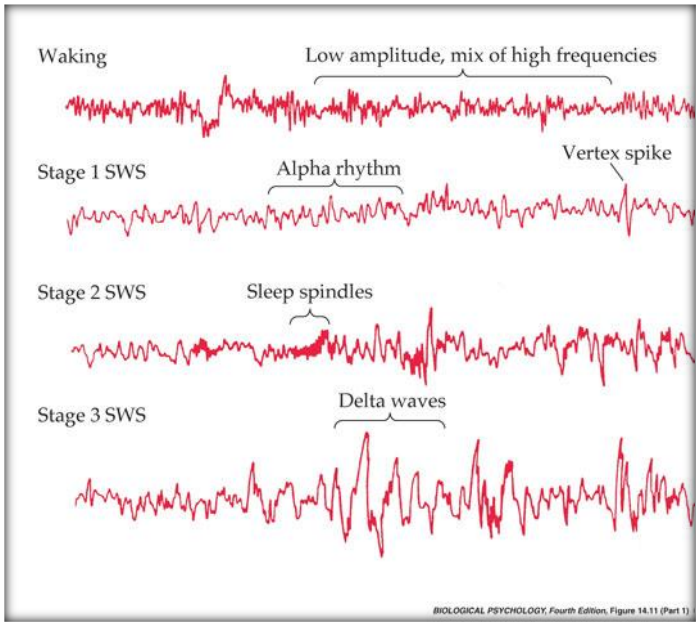
Regulation of Sleep and Wakefulness

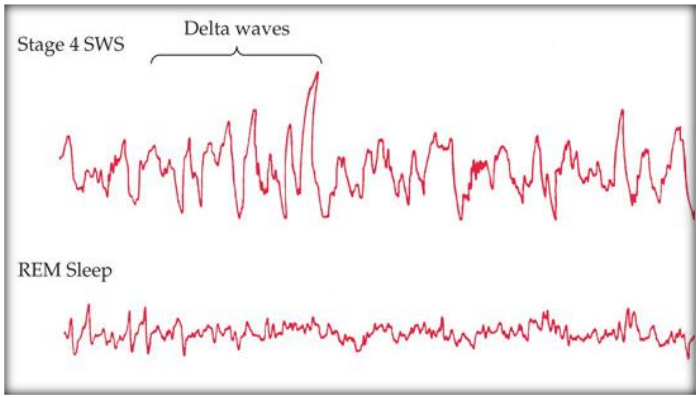
- Two basic intrinsic components
  - 1 Circadian rhythm (process C)
  - 2 Sleep homeostasis (process S),
- Sleep homeostasis is characterized by an increase in sleep pressure following sleep deprivation that is related to the duration of prior wakefulness followed by a decline in sleep need as sleep accumulates.
- Circadian process There are two circadian peaks in wakefulness : one occurring (early evening) and a second peak (late morning). Sleep propensity is least during these peaks of circadian rhythms of arousal Greatest sleep propensity during periods of (overnight between 3:00 and 5:00 am; early-mid afternoon between 3:00 and 5:00 pm).
- Sleep inertia (process W), refers to the short-lived reduction of alertness that occurs immediately following awakening from sleep and disappears within 2 to 4 hours.

Sleep as an active process

- Electroencephalographic (EEG) recordings showed abundant neuronal activity in cortex during sleep
  - Therefore not passive neuronal quiescence
- Pattern of the EEG was very different in sleep than in waking
  - Waves of activity, indicating synchronous firing of cortical neurones
  - Synchronising stimulus coming from sub-cortical areas
  - Reticular formation still seen as important
- Several different levels of sleep
  - Sleep is a complex combination of different aspects

Brain Activity During Sleep





Awake

Low amplitude high frequency EEG

Light sleep

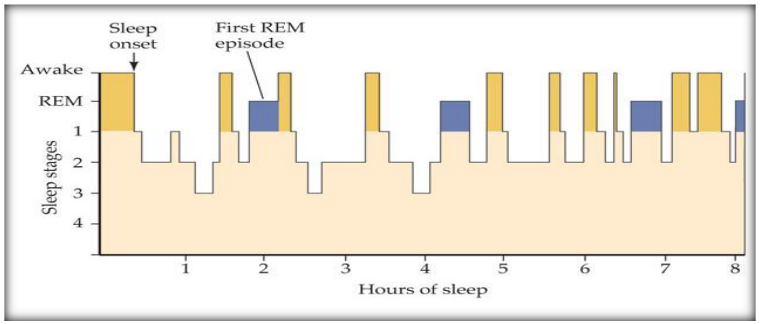
Increasing amplitude decreasing freq. EEG

Deep sleep

High amplitude low frequency EEG

Rapid eye movement (REM) sleep

Low amplitude high frequency EEG



Characteristics of sleep

- Slow-wave sleep = NREM
  - Progressive decrease in spinal reflexes
  - Progressive reduction in heart rate and breathing rate
  - Reduced brain temperature and cerebral blood flow
  - Increased hormone secretion (e.g. growth hormone)
  - Synchronised cortical activity
- REM sleep
  - Spinal reflexes absent
  - Rapid eye movements behind closed eyelids
  - Increased body temperature and cerebral blood flow
  - Desynchronised cortical activity
  - Dreams

Autonomic Nervous System Physiology

- Parasympathetic tone increase and sympathetic tone decrease during NREM sleep.
- During arousals, sympathetic tone increase in bursts.
- During tonic REM sleep, Parasympathetic tone increase even further whereas sympathetic tone reaches its lowest level.
- During phasic REM sleep sympathetic tone transiently increases.
- Muscle tone is maximal during wakefulness but decrease during NREM sleep and decrease even further during REM sleep.
- During REM sleep, myotonic bursts (phasic twitches) as evidenced by intermittent surges in EMG.
- Overall decrease in upper airway dilator muscles during NREM sleep, the reduction is even greater during REM sleep .

Cardio-vascular physiology in sleep

- Heart rate decreases during NREM sleep but fluctuate greatly during REM sleep .
- Brady-tachycardia seen during phasic REM sleep is due to variations of both parasympathetic and sympathetic activities.
- Cardiac output decreases during both NREM and REM sleep.
- Pulmonary blood pressure increases slightly during sleep.
- Arterial blood pressure decreases by 10% during NREM sleep during phasic REM sleep fluctuate due to sympathetic activities.
- Cerebral blood flow decreases 5-20% during NREM sleep during REM sleep an increase in blood flow by up to 40%

Endocrine physiology in sleep

- Melatonin release peaks during sleep.
- Growth hormone peak 90 minutes after sleep onset (closely associated with slow wave sleep).
- Cortisol secretion is independent of sleep. Its peak is in the early morning.
- Thyroid stimulating hormone decreases during sleep.
- Testosterone increases during sleep.
- No relation between GTH ,LH, FSH and sleep .
- Prolactin level increases during sleep.

Brain Mechanisms Controlling Sleep

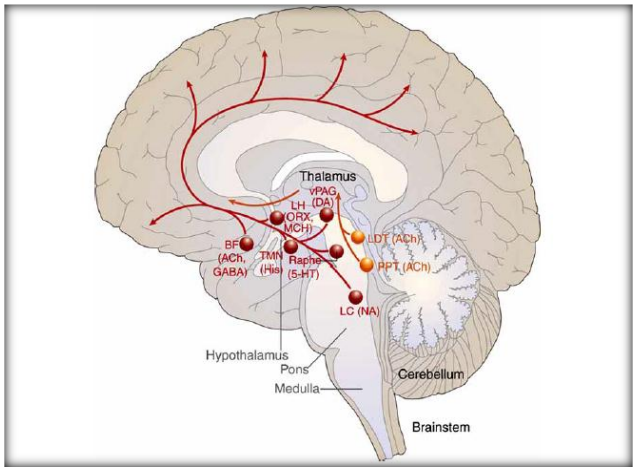
- Sleep is promoted by a complex set of neural and chemical mechanisms
- Daily rhythm of sleep and arousal
  - Supra-chiasmatic nucleus of the hypothalamus (body clock)
  - Pineal gland's secretion of melatonin
- Light is called a Zeitgeber, a German word meaning time-giver because it set the supra-chiasmatic clock
- Altering light/dark cycles produces phase shift and entrainment

In A Nutshell

- The neural circuitry underlying regulation of sleep and wakefulness is discrete yet interdependent.
- Arousal systems that are inhibited by sleep promoting neurons in turn disrupt sleep processes to return to wakefulness.
- Ponto-mesencephalic ascending pathways mediate alertness and cortical arousal of the forebrain.
- One pathway innervates the thalamus and the second extends into the posterior hypothalamus and forebrain.
- Key cell populations within the ascending system are the following:
  - Cholinergic neurons of the pedunculo-pontine and latero-dorsal tegmental nuclei.
  - Noradrenergic neurons from the locus coeruleus.

In A Nutshell

- Serotoninergic neurons from the dorsal and median raphe nuclei.
- Dopaminergic neurons of the ventral peri-aqueductal grey matter.
- Histaminergic neurons of the Tuberomamillary nucleus (TMN).
- Lateral hypothalamic peptidergic neurons containing Melanin Concentrating Hormone or Orexin/ Hypocretin.



The neural circuit of orexin (hypocretin): maintaining sleep and wakefulness

Takeshi Sakurai

- A modest number of cells in the lateral hypothalamus are the sole source of orexin or hypocretin in the human brain.
- Their sprawling projections reach all regions of the arousal network, with the largest being to LC and TMN.
- These neurons fire during wakefulness and are silent during NREM and REM sleep.

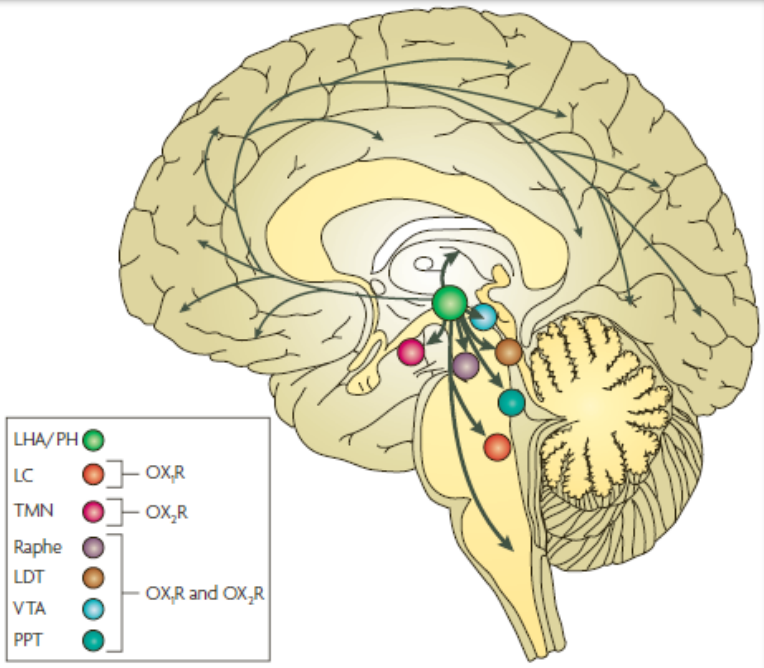


Figure 1 | **Schematic drawing showing main projections of orexin neurons.** This figure summarizes predicted orexinergic projections in the human brain. Please note that distributions of orexin fibres and receptors (OX_1R, OX_2R) are predicted from the results of studies on rodent brains, as it is on rodents that most histological studies on the orexin system have been carried out. Circles show regions with strong receptor expression and dense orexinergic projections. Orexin neurons originating in the lateral hypothalamic area (LHA) and posterior hypothalamus (PH) regulate sleep and wakefulness and the maintenance of arousal by sending excitatory projections to the entire CNS, excluding the cerebellum, with particularly dense projections to monoaminergic and cholinergic nuclei in the brain stem and hypothalamic regions[24–32,38], including the locus coeruleus (LC, containing noradrenaline), tuberomammillary nucleus (TMN, containing histamine), raphe nuclei (Raphe, containing serotonin) and laterodorsal/pedunclopontine tegmental nuclei (LDT/PPT), containing acetylcholine). Orexin neurons also have links with the reward system through the ventral tegmental

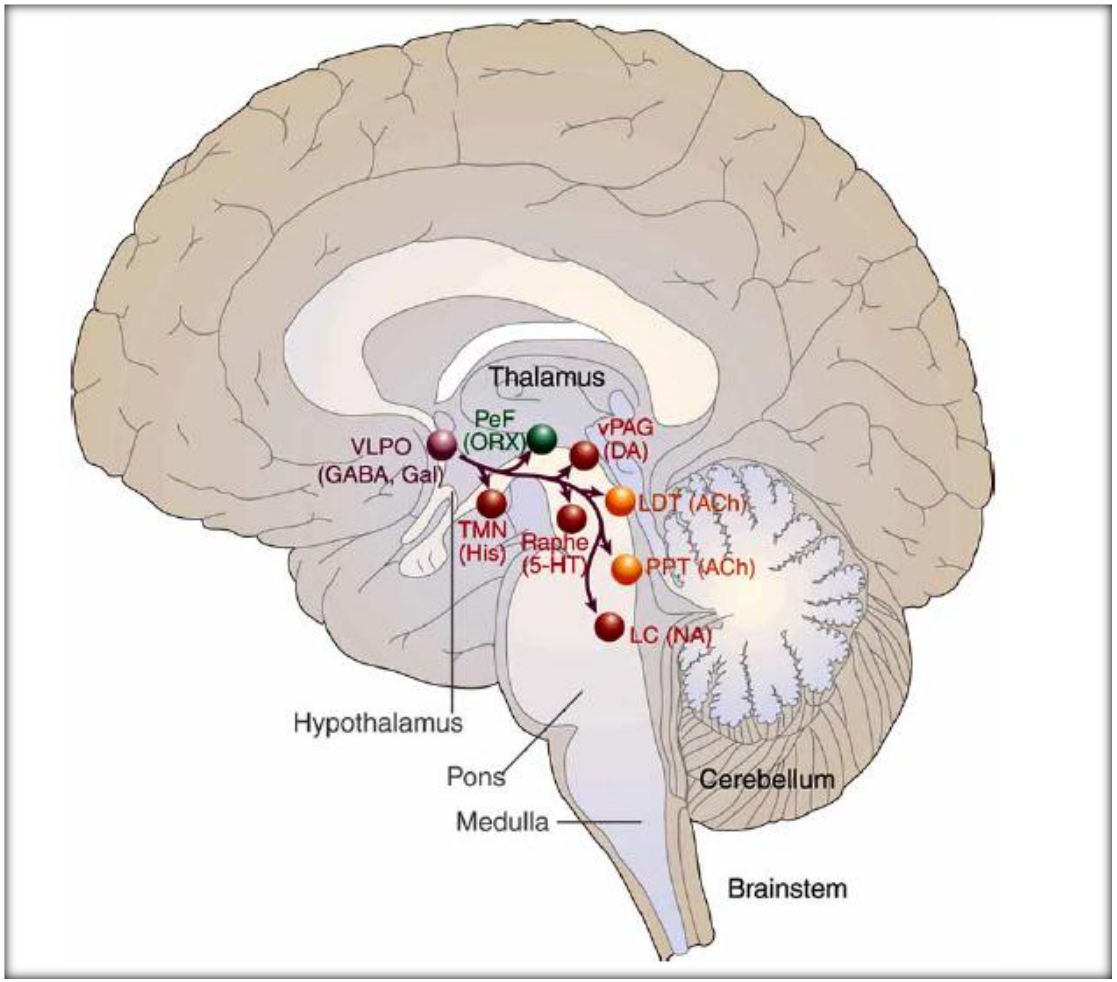
The Ascending Arousal System

- In sum, cholinergic neurons and monoaminergic cells populations form one distinct ascending arousal system, which is paralleled by the second peptidergic arousal system of the orexin/hypocretin nuclei in the lateral hypothalamus.
- These discharge in a coordinated and stereotypic manner, to promote cortical arousal, each making unique but overlapping and somewhat redundant contributions to sustain wakefulness.
- During sleep these circuits are blocked by the neurons of the VLPO.

VLPO efferents secrete GABA & Galanin Inhibitory neurotransmitters

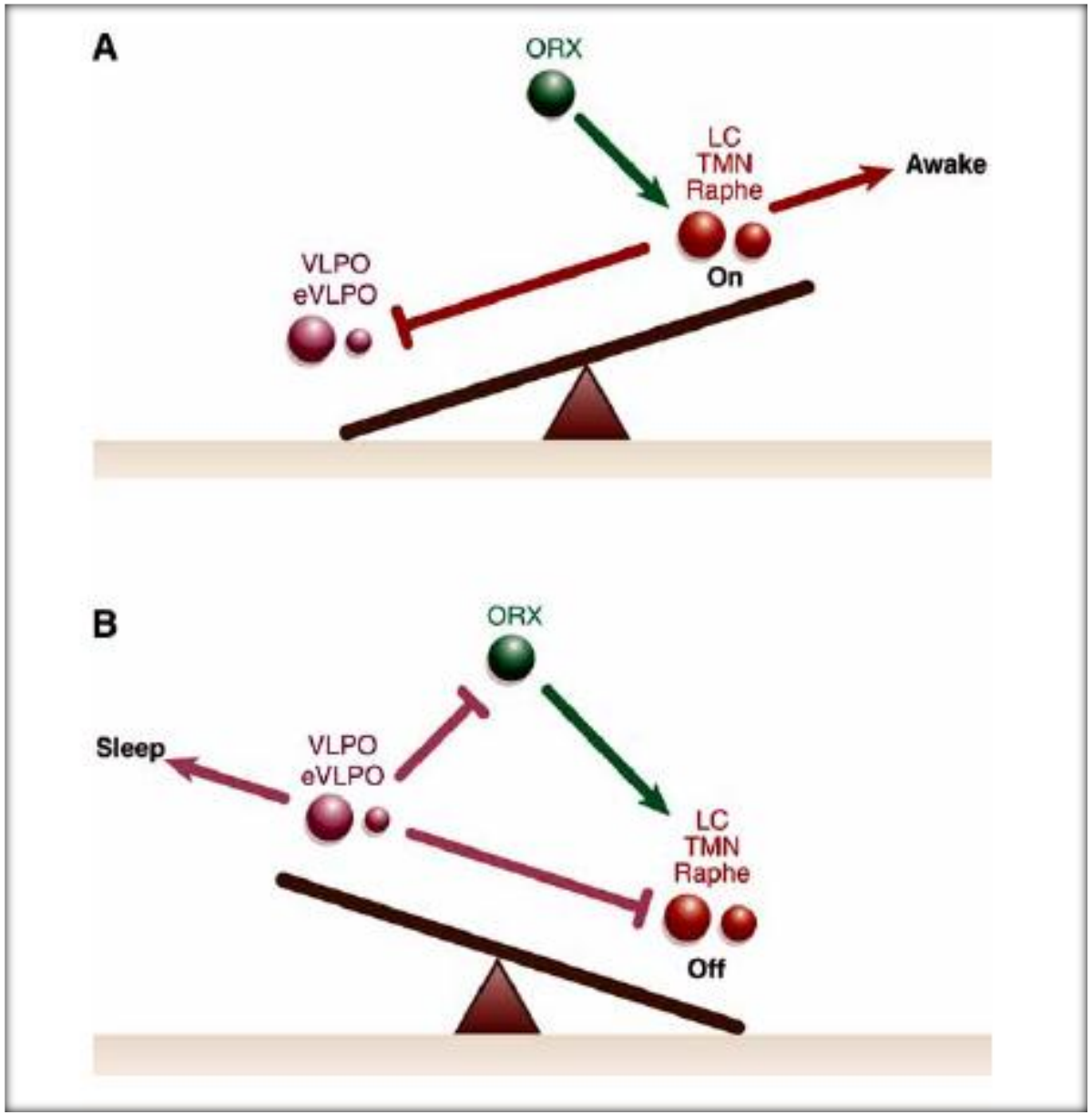
Following experiments by McGinty and colleagues, which demonstrated that lesions in the basal forebrain suppressed sleep in cats [58], Sherin *et al.* determined that a group of ventrolateral preoptic neurons is specifically activated during sleep [107]. Neurons of the VLPO form a dense cluster and also extend more diffusely to innervate the monoaminergic systems in the hypothalamus and brainstem that participate in the modulation of cortical arousal (Fig. **2**). VLPO efferents contain the inhibitory neurotransmitters GABA and galanin, and have been shown to play a central role in the mammalian brain in quieting the ascending monoaminergic arousal system during sleep [36,106].

Projections of VLPO to main components of the ascending arousal system

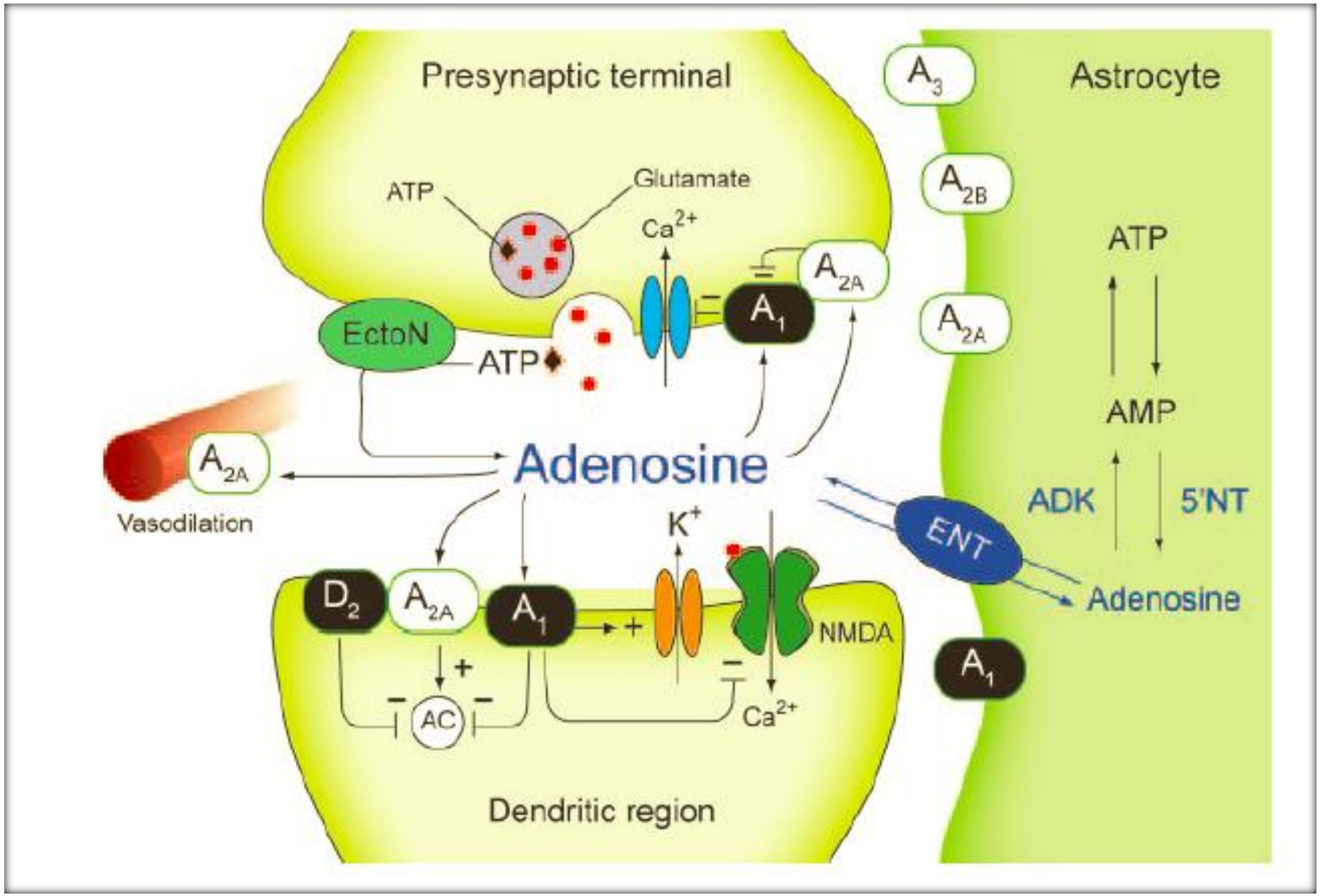


THE BRAINSTEM CONTROL OF STATE STABILITY

The reciprocal inhibitory exchange between the major ascending monoaminergic arousal groups and the sleep-inducing VLPO acts as a feedback loop; when monoamine nuclei discharge intensively during wakefulness, they inhibit the VLPO, and when VLPO fire rapidly during sleep, block the discharge of the monoamine cell groups [98]. This relationship is described as a bistable, "flip-flop" circuit, in which the two halves of the circuit strongly inhibit each other to produce two stable discharge patterns – on or off (Fig. 3). Intermediate states that might be partially "on and off" are resisted. This model helps clarify why sleep-wake transitions are relatively abrupt and mammals spend only about 1% to 2% of the day in a transitional state [99]. Hence, changes between sleep and arousal occur infrequently and


A
ORX
LC
TMN
Raphe
Awake
VLPO
eVLPO
On
B
ORX
Sleep
VLPO
eVLPO
LC
TMN
Raphe
Off

Adenosine & Sleep Induction



Adenosine and sleep–wake regulation

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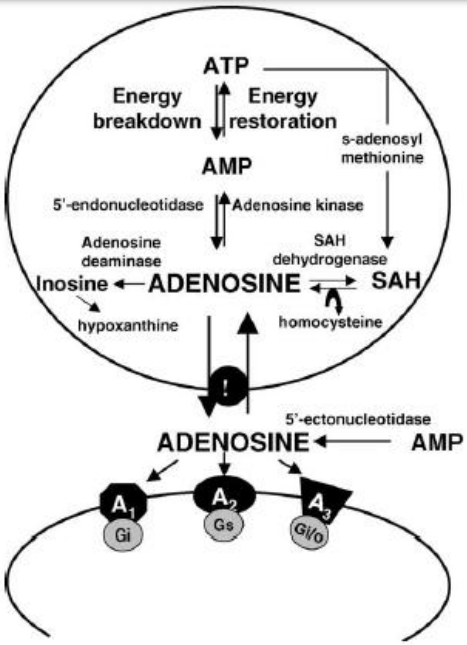

Fig. 6. The biochemical pathway detailing the enzymes responsible for intracellular and extracellular adenosine production as well as its conversion to inositol or phosphorylation to adenosine monophosphate.

Abstract

This review addresses three principal questions about adenosine and sleep–wake regulation: (1) Is adenosine an endogenous sleep factor? (2) Are there specific brain regions/neuroanatomical targets and receptor subtypes through which adenosine mediates sleepiness? (3) What are the molecular mechanisms by which adenosine may mediate the long-term effects of sleep loss? Data suggest that adenosine is indeed an important endogenous, homeostatic sleep factor, likely mediating the sleepiness that follows prolonged wakefulness. The cholinergic basal forebrain is reviewed in detail as an essential area for mediating the sleep-inducing effects of adenosine by inhibition of wake-promoting neurons via the A_1 receptor. The A_{2A} receptor in the subarachnoid space below the rostral forebrain may play a role in the prostaglandin D_2-mediated somnogenic effects of adenosine. Recent evidence indicates that a cascade of signal transduction induced by basal forebrain adenosine A_1 receptor activation in cholinergic neurons leads to increased transcription of the A_1 receptor; this may play a role in mediating the longer-term effects of sleep deprivation, often called sleep debt.

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Behavioral/Systems/Cognitive

Sleep Deprivation Increases A_1 Adenosine Receptor Binding in the Human Brain: A Positron Emission Tomography Study

David Elmenhorst,[1] Philipp T. Meyer,[1] Oliver H. Winz,[1] Andreas Matusch,[1] Johannes Ermert,[2] Heinz H. Coenen,[2,3] Radhika Basheer,[4] Helmut L. Haas,[5] Karl Zilles,[1,3] and Andreas Bauer[1,3]

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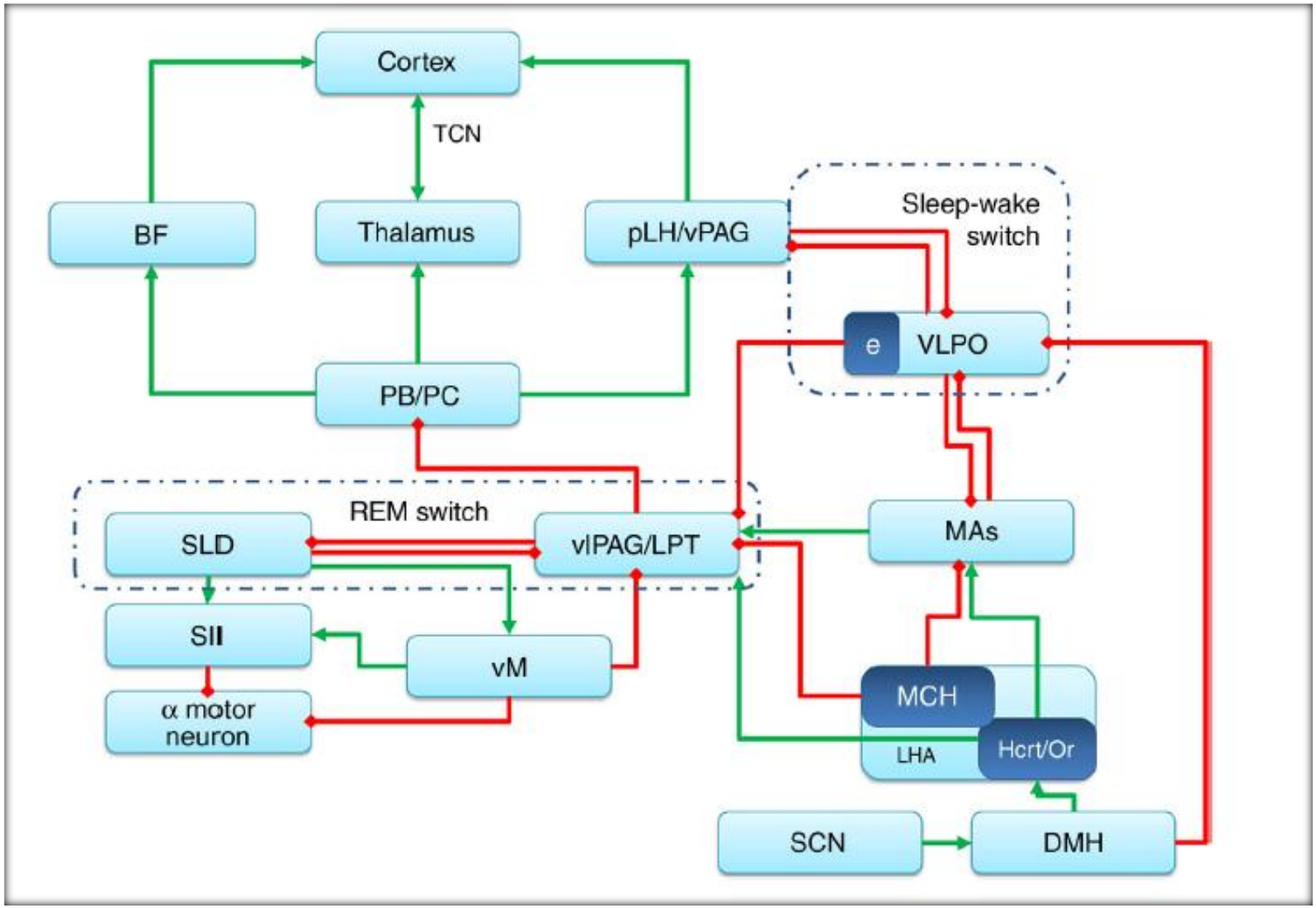
It is currently hypothesized that adenosine is involved in the induction of sleep after prolonged wakefulness. This effect is partially reversed by the application of caffeine, which is a nonselective blocker of adenosine receptors. Here, we report that the most abundant and highly concentrated A_1 subtype of cerebral adenosine receptors is upregulated after 24 h of sleep deprivation. We used the highly selective A_1 adenosine receptor (A_1AR) radioligand [^{18}F]CPFPX ([^{18}F]8-cyclopentyl-3-(3-fluoropropyl)-1-propylxanthine) and quantitative positron emission tomography to assess cerebral A_1ARs before and after sleep deprivation in 12 healthy volunteers and a control group ($n = 10$) with regular sleep. In sleep deprived subjects, we found an increase of the apparent equilibrium total distribution volume in a region-specific pattern in all examined brain regions with a maximum increase in the orbitofrontal cortex (15.3%; $p = 0.014$). There were no changes in the control group with regular sleep. This is the first molecular imaging study that provides *in vivo* evidence for an A_1AR upregulation in cortical and subcortical brain regions after prolonged wakefulness, indicating that A_1AR expression is contributing to the homeostatic sleep regulation.

Key words: imaging; adenosine A_1 receptor; positron emission tomography; [^{18}F]CPFPX; sleep deprivation; human

Components Of Sleep-Wake Circuitry



I've always envied people who sleep easily. Their brains must be cleaner, the floorboards of the skull well swept, all the little monsters closed up in a steamer trunk at the foot of the bed.

David Benioff

“If sleep does not serve some vital function, it is the biggest mistake evolution ever made”-

Allan Rechtschaffen

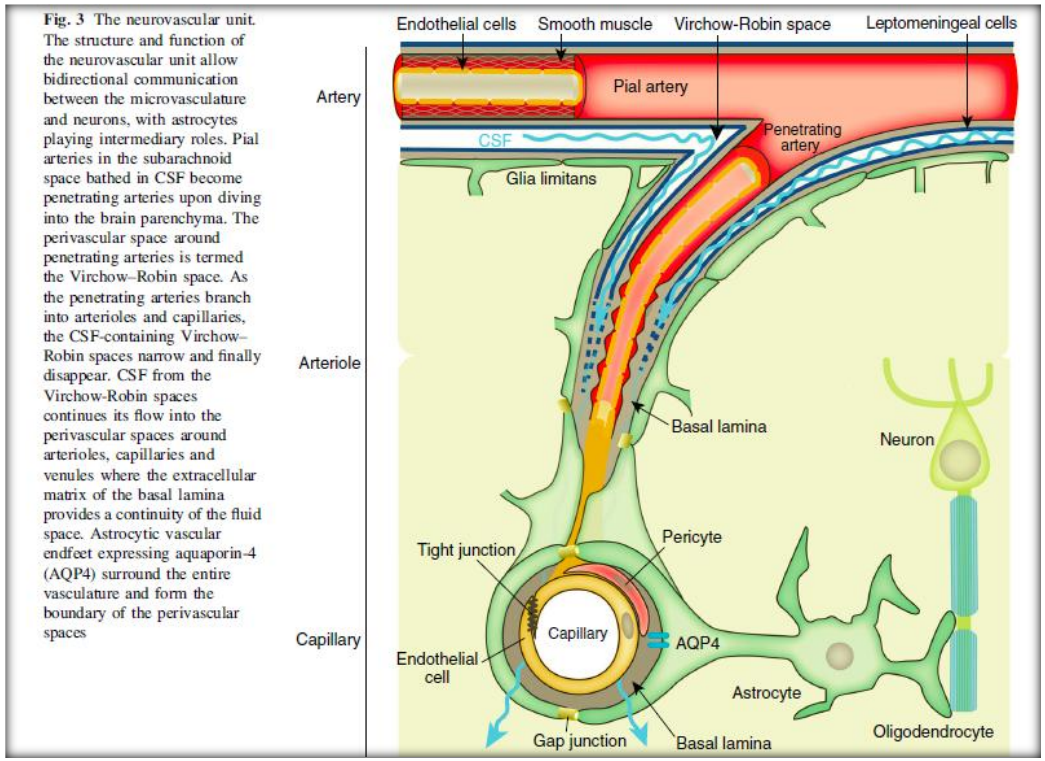
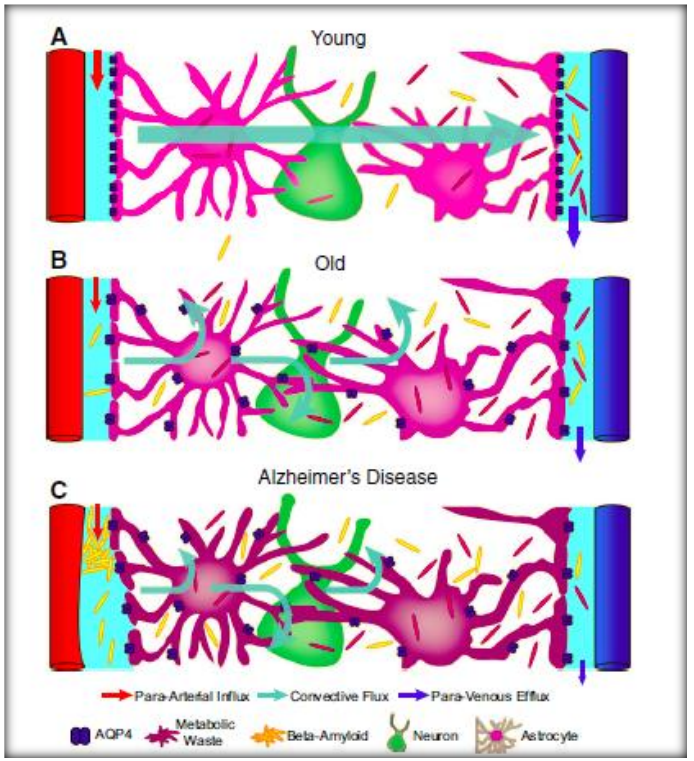


Fig. 3 The neurovascular unit. The structure and function of the neurovascular unit allow bidirectional communication between the microvasculature and neurons, with astrocytes playing intermediary roles. Pial arteries in the subarachnoid space bathed in CSF become penetrating arteries upon diving into the brain parenchyma. The perivascular space around penetrating arteries is termed the Virchow–Robin space. As the penetrating arteries branch into arterioles and capillaries, the CSF-containing Virchow–Robin spaces narrow and finally disappear. CSF from the Virchow-Robin spaces continues its flow into the perivascular spaces around arterioles, capillaries and venules where the extracellular matrix of the basal lamina provides a continuity of the fluid space. Astrocytic vascular endfeet expressing aquaporin-4 (AQP4) surround the entire vasculature and form the boundary of the perivascular spaces



Sleep Functions: Waste Debridement, Memory Consolidation & Emotional Salience

The Glymphatic System: A Beginner's Guide

Nadia Aalling Jessen[1] · Anne Sofie Finmann Munk[1] · Iben Lundgaard[1] · Maiken Nedergaard[1]

Garbage Truck of the Brain

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Brain may flush out toxins during sleep

NIH-funded study suggests sleep clears brain of damaging molecules associated with neurodegeneration

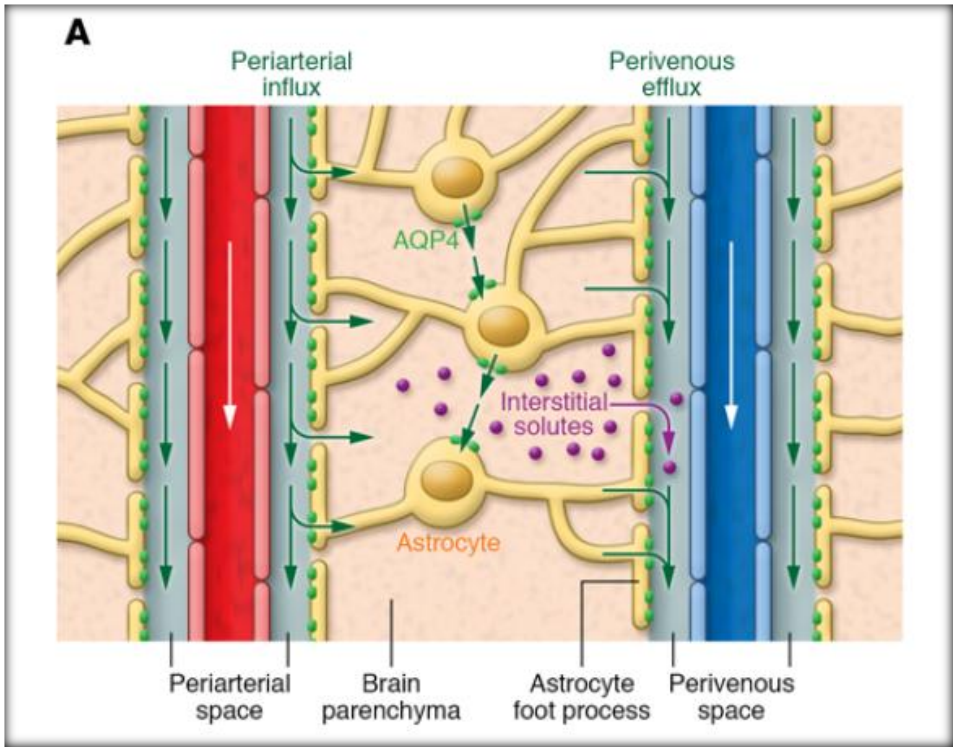
A good night's rest may literally clear the mind. Using mice, researchers showed for the first time that the space between brain cells may increase during sleep, allowing the brain to flush out toxins that build up during waking hours. These results suggest a new role for sleep in health and disease. The study was funded by the National Institute of Neurological Disorders and Stroke (NINDS), part of the NIH.

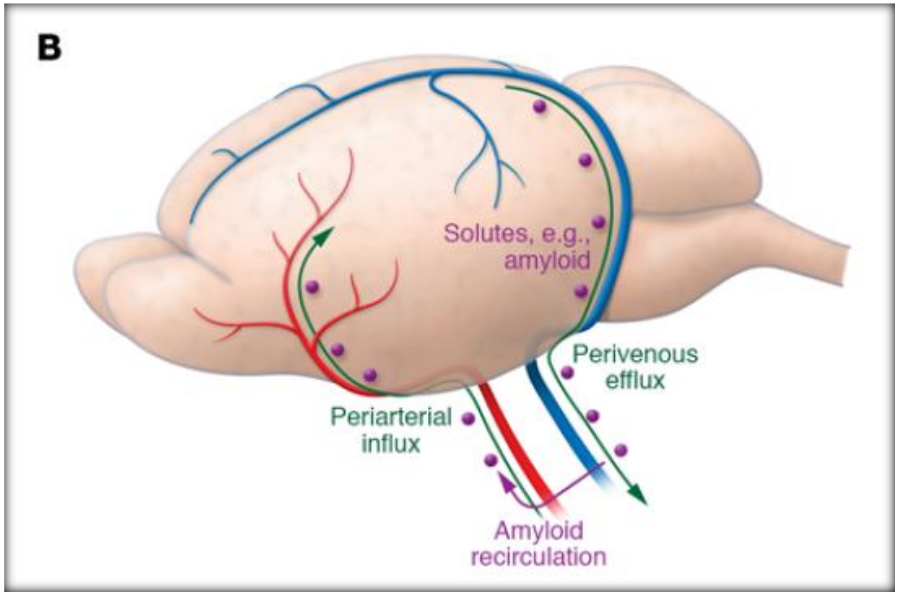
"Sleep changes the cellular structure of the brain. It appears to be a completely different state," said Maiken Nedergaard, M.D., D.M.Sc., co-director of the Center for Translational Neuromedicine at the University of Rochester Medical Center in New York, and a leader of the study.

For centuries, scientists and philosophers have wondered why people sleep and how it affects the brain. Only recently have scientists shown that sleep is important for storing memories. In this study, Dr. Nedergaard and her colleagues unexpectedly found that sleep may be also be the period when the brain cleanses itself of toxic molecules.

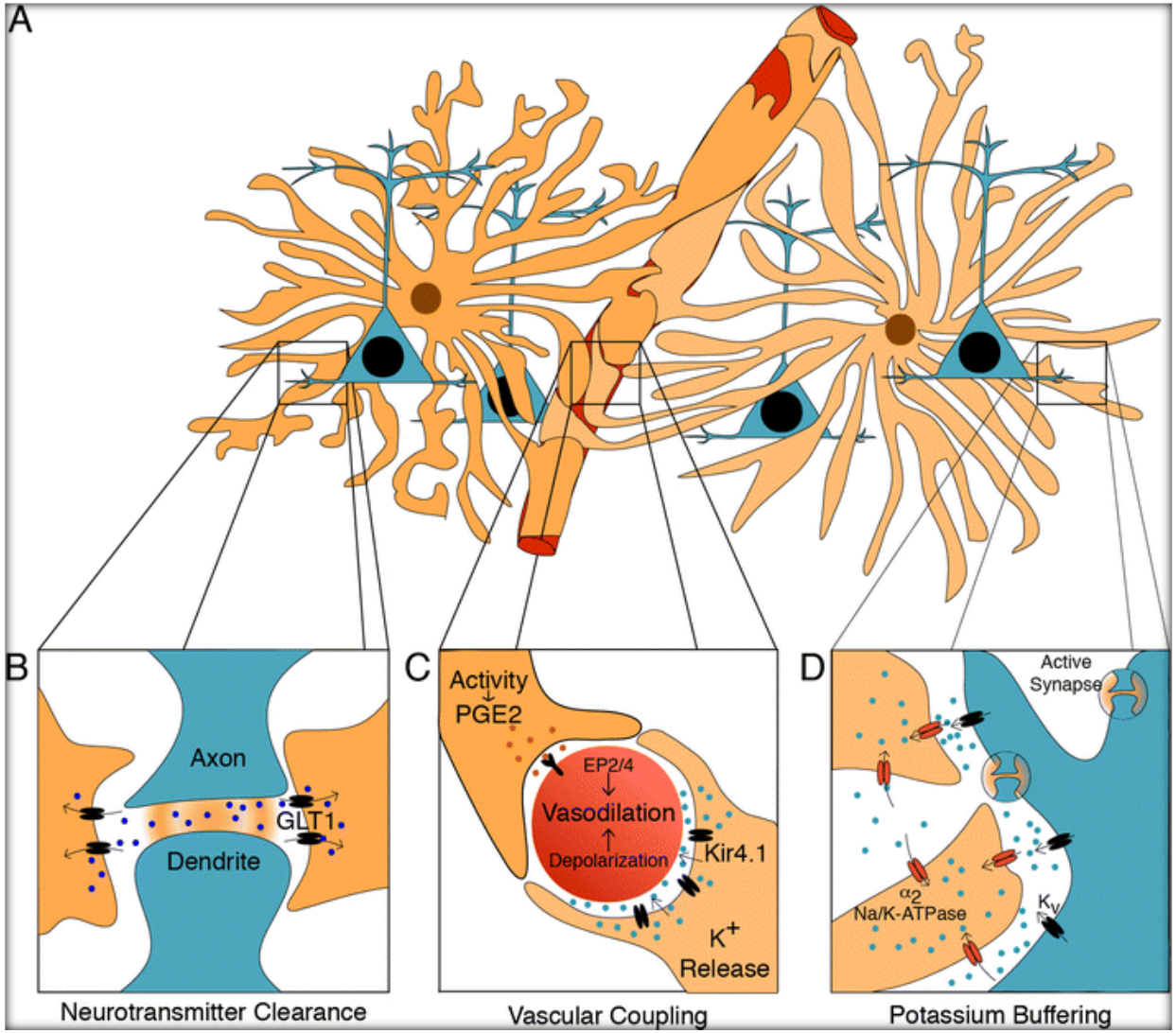
Glymphatic Insights In A Nutshell

- Unidirectional flow of CSF along the interstitium mediated by the glymphatics occurs only in sleep and it abates on arousal (mediated by adrenergic tone)
- Supine and lateral sleeping postures optimize glymphatic function and prone sleeping reduces efficiency by 40%
- Voluntary exercise and low dose alcohol enhance glymphatic efficiency
- Head injury, diabetes mellitus, strokes (especially lacunar), and obstructive sleep apnoea impair glymphatic efficiency
- Glymphatic function excretes beta-amyloid and tau in normal asymptomatic individuals


A
Periarterial influx
Perivenous efflux
AQP4
Interstitial solutes
Astrocyte
Periarterial space
Brain parenchyma
Astrocyte foot process
Perivenous space


B
Solutes, e.g., amyloid
Perivenous efflux
Periarterial influx
Amyloid recirculation

Astrocyte Functions in Sleep



The Astrocyte: A Quiet But Industrious Renovator In Sleep

- The unidirectional flow of CSF during glymphatic activation in sleep is mediated by a gating structure, Aquaporin-4 located on the foot process of the astrocyte.
- The sleep homeostasis driven by adenosine accumulation is dependent on astrocytic production and streaming onto A1R adenosine receptors.
- Astrocytes also regulate neuronal slow oscillations in cortical pyramidal cells.
- ANLS: astrocytes take up glucose, metabolize it to lactate and shuttle it to neurons via mono-carboxylate transporters.
- This is pivotal for sleep associated memory consolidation.

Amyloid-β Dynamics are Regulated by Orexin and the Sleep-Wake Cycle

Jae-Eun Kang[1], Miranda M. Lim[1], Randall J. Bateman[1,2,3], James J. Lee[1], Liam P. Smyth[1], John R. Cirrito[1,2], Nobuhiro Fujiki[5], Seiji Nishino[5], and David M. Holtzman[1,2,3,4,*]

NEUROLOGICAL DISORDERS

The Relationship between Sleep Quality and Brain Amyloid Burden

Belinda M. Brown, PhD[1,2,*]; Stephanie R. Rainey-Smith, PhD[1,2,*]; Victor L. Villemagne, MD[3]; Michael Weinborn, PhD[1,2,4]; Romola S. Bucks, PhD[4]; Hamid R. Sohrabi, PhD[1,2]; Simon M. Laws, PhD[1,2]; Kevin Taddei, BSc[1,2]; S. Lance Macaulay, PhD[5]; David Ames, MD[6,7]; Christopher Fowler, PhD[8]; Paul Maruff, PhD[8,9]; Colin L. Masters, MD[8]; Christopher C. Rowe, MD[3]; Ralph N. Martins, PhD[1,2,10]; and the AIBL Research Group[11]

Significance

Sleep disruption increases with advancing age, and has previously been associated with increased Alzheimer disease pathology in numerous animal studies. However, to date, few human studies have evaluated the relationship between sleep and brain beta-amyloid burden (an indicator of Alzheimer disease pathology) in a highly characterised cohort. Thus, in the current study we have evaluated the relationship between self-reported sleep factors and brain beta-amyloid burden in a cohort of 184 cognitively healthy older adults. We report an association between longer sleep latency and higher levels of brain beta-amyloid burden. Previous reports suggest the relationship between sleep and beta-amyloid is likely bi-directional; thus, future longitudinal studies are essential to further understand this relationship.

Poor sleep is associated with CSF biomarkers of amyloid pathology in cognitively normal adults

Results: Worse subjective sleep quality, more sleep problems, and daytime somnolence were associated with greater AD pathology, indicated by lower CSF Aβ42/Aβ40 and higher t-tau/Aβ42, p-tau/Aβ42, MCP-1/Aβ42, and YKL-40/Aβ42. There were no significant associations between sleep and NFL or neurogranin.

Conclusions: Self-report of poor sleep was associated with greater AD-related pathology in cognitively healthy adults at risk for AD. Effective strategies exist for improving sleep; therefore sleep health may be a tractable target for early intervention to attenuate AD pathogenesis.

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β-Amyloid accumulation in the human brain after one night of sleep deprivation

Ehsan Shokri-Kojori[a,1], Gene-Jack Wang[a,1], Corinde E. Wiers[a], Sukru B. Demiral[a], Min Guo[a], Sung Won Kim[a], Elsa Lindgren[a], Veronica Ramirez[a], Amna Zehra[a], Clara Freeman[a], Gregg Miller[a], Peter Manza[a], Tansha Srivastava[a], Susan De Santi[b], Dardo Tomasi[a], Helene Benveniste[c], and Nora D. Volkow[a,1]

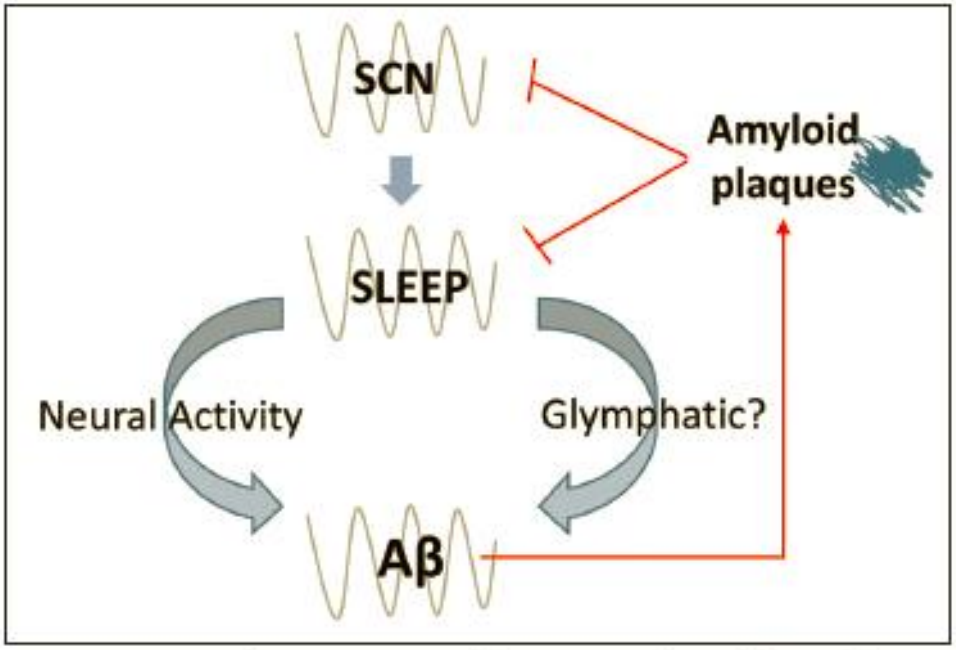

Figure. From studies in mice and humans it is hypothesized that neural and glymphatic activity during sleep are involved in release of amyloid-β (Aβ), which when converted to amyloid plaques has an inhibitory impact on sleep.

Sleep Is for Forgetting

Gina R. Poe
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It is possible that one of the essential functions of sleep is to take out the garbage, as it were, erasing and "forgetting" information built up throughout the day that would clutter the synaptic network that defines us. It may also be that this cleanup function of sleep is a general principle of neuroscience, applicable to every creature with a nervous system.

Key words: depotentiation; development; mental health; noradrenaline; REM sleep; spindles; theta; TR sleep

Dual Perspectives Companion Paper: Sleep Is for Forgetting, by Gina R. Poe

Sleep to Remember

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Scientific investigation into the possible role of sleep in memory consolidation began with the early studies of Jenkins and Dallenbach (1924). Despite nearly a century of investigation with a waxing and waning of interest, the role of sleep in memory processing remains controversial and elusive. This review provides the historical background for current views and considers the relative contribution of two sleep states, rapid eye movement sleep and slow-wave sleep, to offline memory processing. The sequential hypothesis, until now largely ignored, is discussed, and recent literature supporting this view is reviewed.

Synaptic Homeostatic Hypothesis

In this respect, the default assumption among neuroscientists has been that synaptic homeostasis is maintained during learning itself, when the brain is online. SHY, instead, proposes that synaptic renormalization should not happen during waking, when we are at the mercy of a particular environment and slaves of the "here and now," but during sleep, when the brain is offline. Freed from the tyranny of its immediate environment, the brain can sample all its memories—old and new—and renormalize the total amount of synaptic strength in a smart way, preserving and consolidating those newly formed memory traces that fit best with its overall knowledge basis, while forgetting those that fit less well. Thus, sleep should be a time for net synaptic depression, leading to optimal "down-selection" of memory traces.

The Functional Role of Dreaming in Emotional Processes

*Serena Scarpelli, Chiara Bartolacci, Aurora D'Atri, Maurizio Gorgoni and Luigi De Gennaro**

Department of Psychology, Sapienza University of Rome, Rome, Italy

Here, we outlined that dreaming during REM sleep may have a pivotal role in the emotional regulation and emotional memory consolidation, accordingly with some previous works (e.g., Cartwright et al., 1998; Desseilles et al., 2011). The current

Dahl, 1996; Gujar et al., 2011). Although disentangling the issue is out of our purpose, undoubtedly, REM sleep alterations are responsible of emotional imbalance and the maintenance of REM sleep promotes adaptive emotional responses during waking life

The Functions Of Human Sleep

- Several studies reveal that NREM sleep is responsible for memory consolidation, a complex process that involves transfer of data from temporary storage in the hippocampus that occurs in daytime to permanent storage in the frontal and parietal neocortices. This occurs during the phase of slow wave sleep, reflected in the EEG as sleep spindles and K complexes.
- Recent studies imply that REM sleep is responsible for emotional salience/health, and REM deprivation produces anxiety and cyclothymic mood dysfunction. REM consolidates emotional memories
- The final function of sleep is waste clearance of brain metabolites, e.g. amyloid and tau via the GLYMPHATIC SYSTEM, activated exclusively in sleep and suppressed during wakefulness.

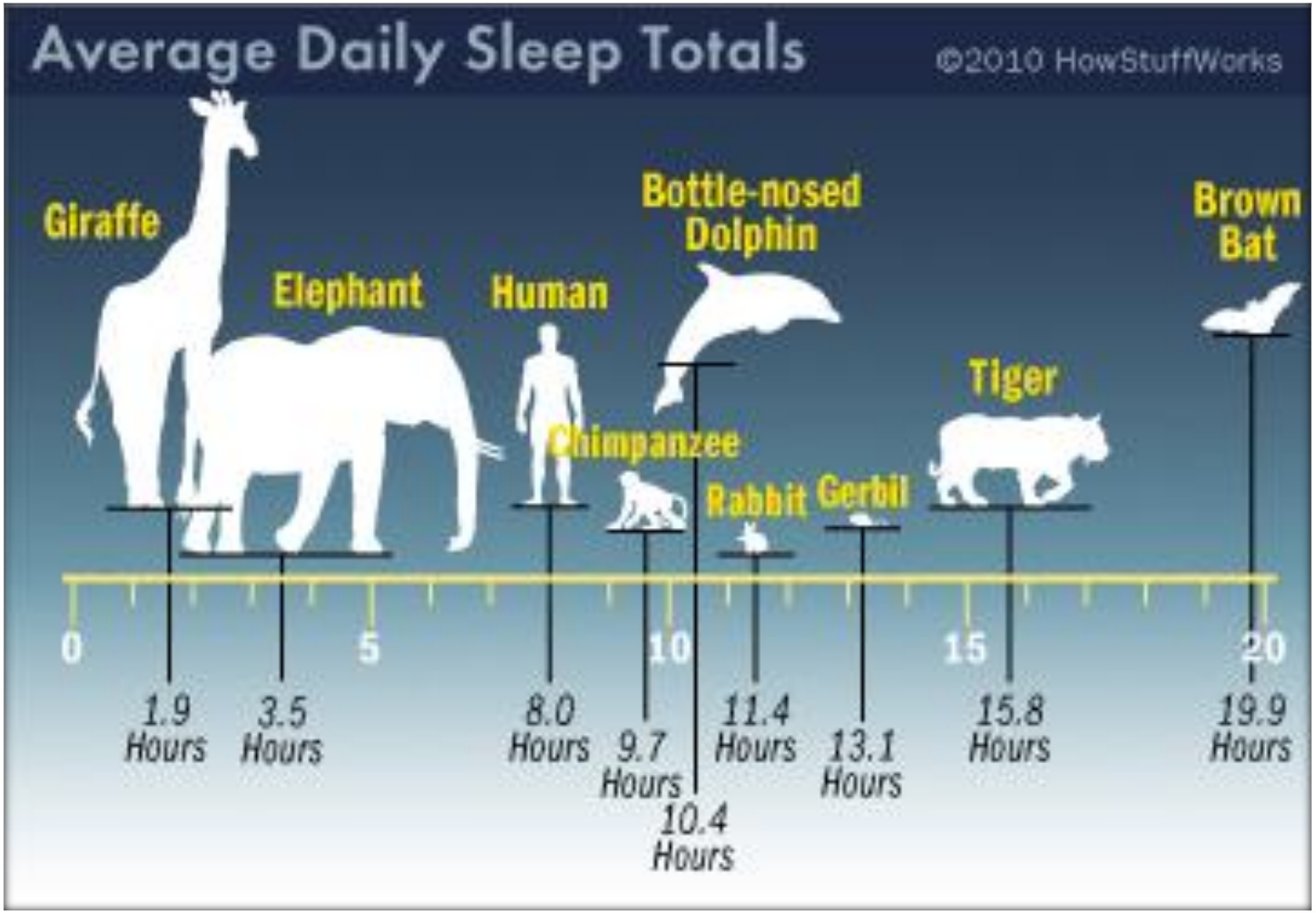
The Functions Of Human Sleep

- The Synaptic Homeostatic Hypothesis: postulates that the key function of sleep is to prune and sculpt synapses acquired during daytime cerebral experiences and functioning from a large collection of all data to a moulded and useful archive of synapses which will constitute memories of the daytime experiences.
- These memories to be archived and stored are selected by a process being understood as based on thresholds of synaptic frequency and intensity. The actual regulatory processes are not fully understood.
- This integrates processes of restoration and repair of CNS architecture.

Sleep functions

- Memory consolidation.
- Emotional Salience.
- Protective behavioral adaptation
- Biochemical waste debridement: beta-amyloid & phosphorylated tau.
- Energy conservation.
- Body growth: restorative physiology.
- Regulation of immune function: NK cells
- Energy Homeostasis and weight regulation

Animal Kingdom Sleep Duration



Uni-hemispheric Slow Wave Sleep

- A phenomenon observed in the animal and avian kingdom wherein survival requires a watch-out for predators during sleep
  - Dolphins
  - Whales
  - Porpoises
  - Manatees
  - Fur Seal
  - Sea Lion
  - Numerous Bird Species

Report

Current Biology

Night Watch in One Brain Hemisphere during Sleep Associated with the First-Night Effect in Humans

Highlights

- Interhemispheric asymmetry in sleep depth occurs for the first night in a new place
- This interhemispheric asymmetry occurs in the default-mode network
- The less-asleep hemisphere shows increased vigilance in response to deviant stimuli
- One brain hemisphere may work as a night watch during sleep in a novel environment

Authors

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In Brief

Tamaki et al. find that when humans sleep in a novel environment, the default-mode network in one hemisphere is kept more vigilant to wake the sleeper up as a night watch upon detection of deviant stimuli. The regional interhemispheric asymmetric sleep in a novel environment may play a similar protective role to that in marine mammals and birds.

The Effects of Sleep Deprivation

- Excessive daytime drowsiness
- Impaired memory and cognitive functioning: loss of speech fluency, risk assessment failure, inability to appreciate humour
- Higher vulnerability to seizures despite compliance with AEDs
- Increase in generalized anxiety and vulnerability to extreme irritability: Chronically could lead to psychosis
- Altered immunological competence and enhanced risk of immune mediated disorders
- Change in dynamics of leptin, ghrelin, ad resultant risk of obesity and insulin resistance and atherosclerosis

Severe Sleep Deprivation Causes Hallucinations and a Gradual Progression Toward Psychosis With Increasing Time Awake

Flavie Waters[1,2], *Vivian Chiu*[1,3], *Amanda Atkinson*[2] *and Jan Dirk Blom*[4,5,6*]

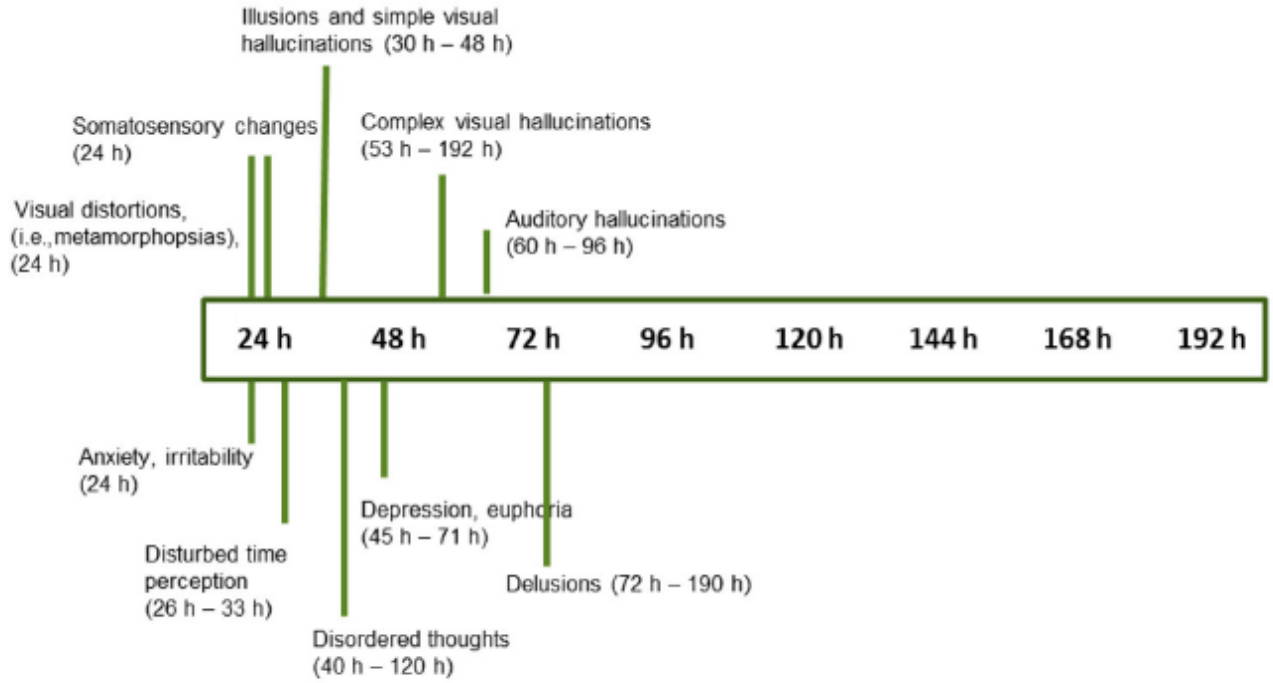

FIGURE 4 | Progression of symptom onset as a function of wakefulness duration, with time range at which symptoms were first reported ($n = 18$ studies, see text for references).

Severe Sleep Deprivation Causes Hallucinations and a Gradual Progression Toward Psychosis With Increasing Time Awake

Flavie Waters[1,2], *Vivian Chiu*[1,3], *Amanda Atkinson*[2] *and Jan Dirk Blom*[4,5,6*]

Conclusions: Psychotic symptoms develop with increasing time awake, from simple visual/somatosensory misperceptions to hallucinations and delusions, ending in a condition resembling acute psychosis. These experiences are likely to resolve after a period of sleep, although more information is required to identify factors which can contribute to the prevention of persistent symptoms.

Keywords: sleep restriction, homeostatis, hallucination, delusion, illusion, distortion, metamorphopsia, misperception

EDITORIAL

Hyperalgesia Induced by REM Sleep Loss: A Phenomenon in Search of a Mechanism

Comment on: Roehrs T; Hyde M; Blaisdell B et al. Sleep loss and REM sleep loss are hyperalgesic. *SLEEP* 2006; 29(2):145-151.

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Roles of Microglial Phagocytosis and Inflammatory Mediators in the Pathophysiology of Sleep Disorders

*Agnes Nadjar [1, 2, 3], Henna-Kaisa M. Wigren [4] and Marie-Eve Tremblay [5, 6]**

Cellular/Molecular

Sleep Loss Promotes Astrocytic Phagocytosis and Microglial Activation in Mouse Cerebral Cortex

Michele Bellesi,[1,2] Luisa de Vivo,[1] Mattia Chini,[1] Francesca Gilli,[3] Giulio Tononi,[1] and Chiara Cirelli[1]

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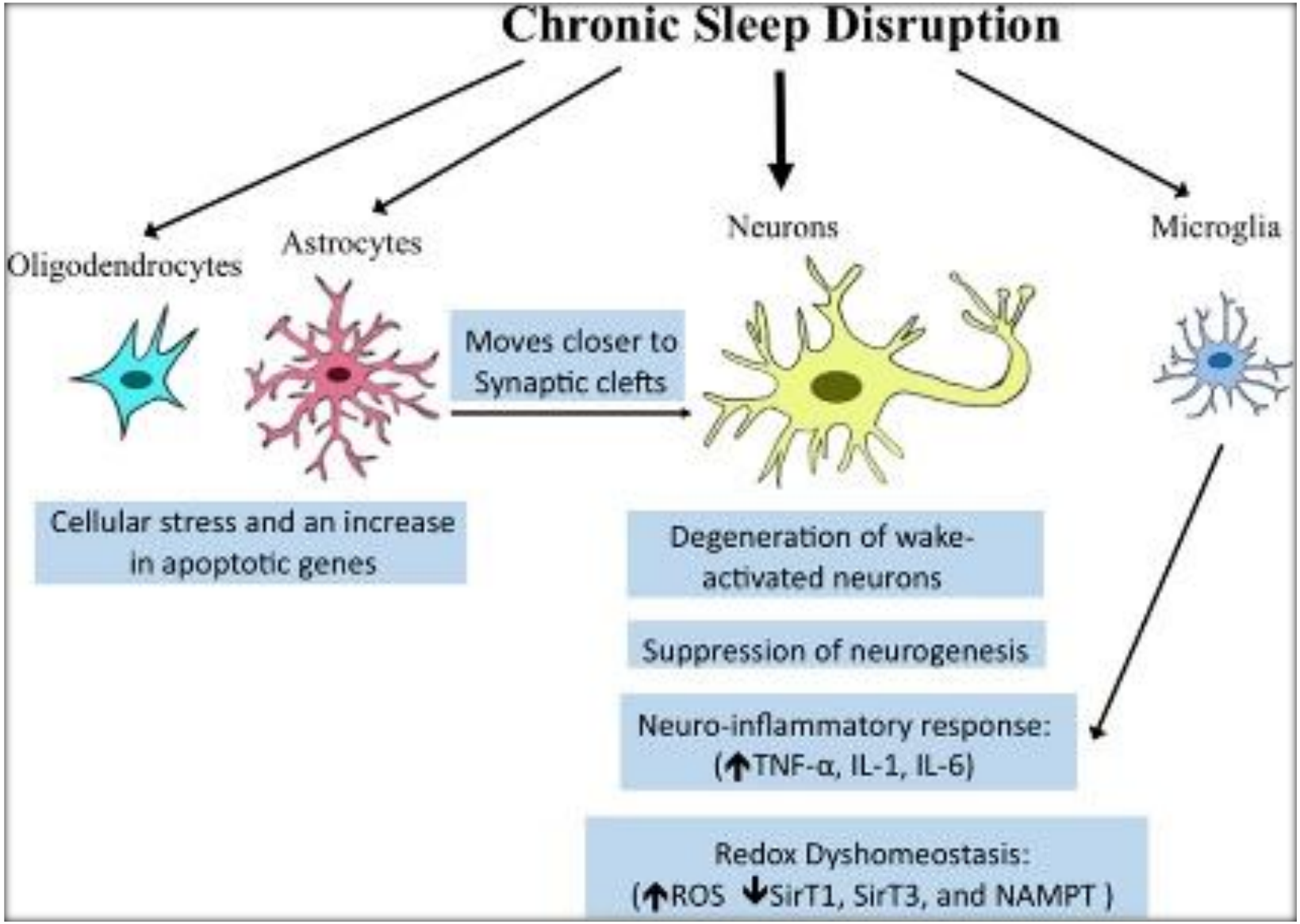

Chronic Sleep Disruption
Oligodendrocytes
Astrocytes
Neurons
Microglia
Moves closer to Synaptic clefts
Cellular stress and an increase in apoptotic genes
Degeneration of wake-activated neurons
Suppression of neurogenesis
Neuro-inflammatory response: (↑TNF-α, IL-1, IL-6)
Redox Dyshomeostasis: (↑ROS ↓SirT1, SirT3, and NAMPT)

The Association Between Sleep Duration and Leptin, Ghrelin, and Adiponectin Among Children and Adolescents

Erika W. Hagen[1] · Samuel J. Starke[2] · Paul E. Peppard[3]

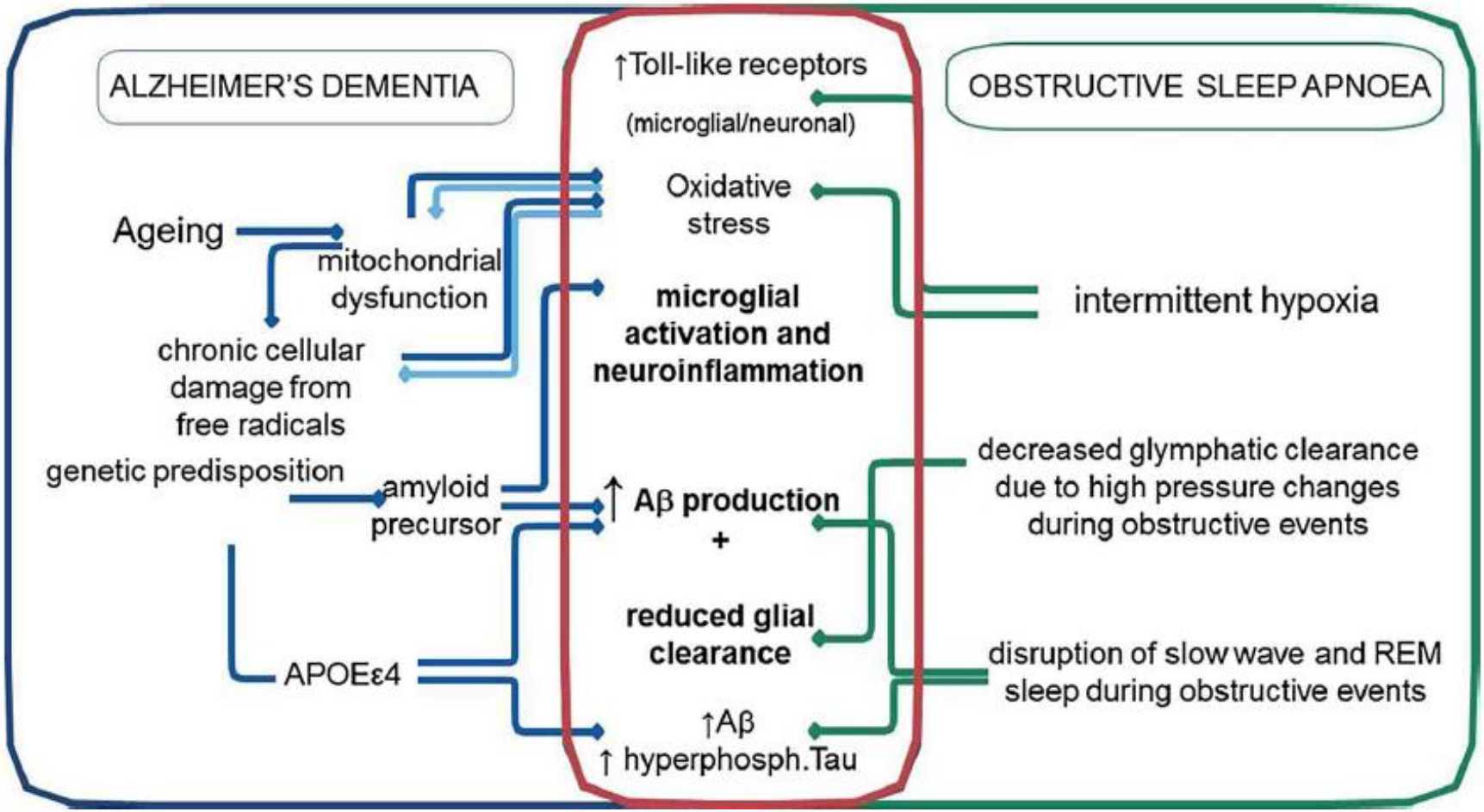
mones. In this review, we summarized evidence addressing the latter hypothesized mechanism, focusing on three specific hormones—leptin, ghrelin, and adiponectin—in children. Consistent associations between short sleep and reduced levels of the adipocyte-derived hormones leptin and adiponectin, or elevated levels of the gut-derived hormone ghrelin, would provide evidence consistent with a hormone-mediated mechanistic link between short sleep and weight gain. Unfortunately, the

A single night of sleep deprivation increases ghrelin levels and feelings of hunger in normal-weight healthy men

SEBASTIAN M. SCHMID[1], MANFRED HALLSCHMID[2], KAMILA JAUCH-CHARA[3], JAN BORN[2] and BERND SCHULTES[1,4]

Departments of [1]Internal Medicine I, [2]Neuroendocrinology and [3]Psychiatry and Psychotherapy, University of Luebeck, Luebeck, Germany and [4]Interdisciplinary Obesity Center, Kantonsspital St Gallen, Rorschach, Switzerland

Alzheimer's Disease & OSA: shared pathogenicity



Update on Obstructive Sleep Apnea: Implications for Neuropsychiatry

Christopher A. Baker, Psy.D., Robin A. Hurley, M.D, Katherine Taber, Ph.D.

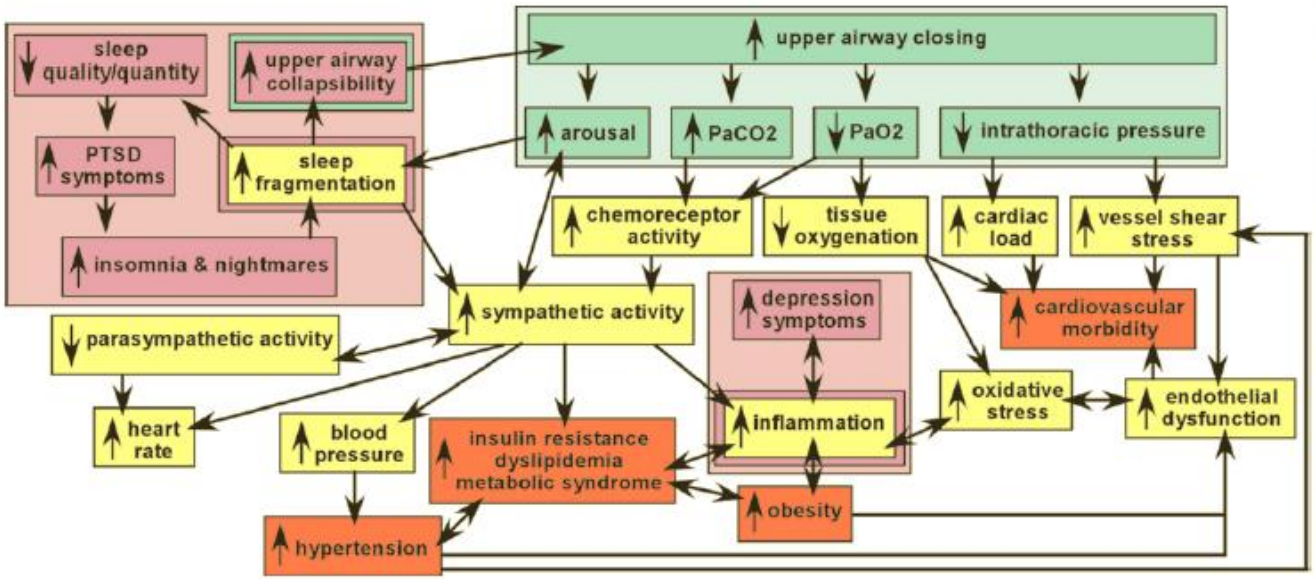


FIGURE 1. Intermittent upper airway closings are the defining event in obstructive sleep apnea (OSA). The major physiological changes (blue green) that occur as a result, and some of the acute (yellow) and chronic (orange) adverse effects are diagramed below.[1–3] Proposed bidirectional relationships between specific psychiatric conditions (purple) and specific acute and/or chronic adverse effects of OSA are also illustrated.[4–9] These complex interrelationships indicate the potential for multiple deleterious interactions between OSA and comorbid psychiatric disorders, and/or medical conditions, supporting the importance of early recognition and treatment.

Take Home Messages

- The neuroscience of sleep has undergone a revolutionary understanding of its fundamental biological basis, and the anatomical basis of its key postulated purpose.
- There has been an explosion in scientific endeavours to unravel the pathological consequences of poor sleep physiology.
- Sleep aberrations are perceived as an acquired lifestyle disorder of these current times that may lead to neurological holocaust within a few decades.
- ‘Winter is truly coming’ if we ignore/disregard sleep physiology.

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