# Understanding of Sleep and Importance of its Stages

## A Review Article

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# ABSTRACT OF the REVIEW ARTICLE


# Understanding of Sleep and Importance of its Stages

Besides eating, drinking and breathing, sleeping comes to be one of the pillars for us to have a good mental and physical health. On average, we spend approximately a third of our life asleep. Sleep is a complex physiological process that plays an intrinsic part in many behavioral and physiological functions. It is regulated by both cellular and molecular mechanisms under the control of homeostasis and circadian rhythm processes. It occurs to some extent in all animals, although sleep expression in lower animals may be co-extensive with rest. Currently, all researchers agree with the fact that says there is no single physiological role sleep serves. Nevertheless, it is quite evident that sleep is essential for many vital functions including development, energy conservation, brain waste clearance, modulation of immune responses, cognition, performance, vigilance, disease, and psychological state.

In humans, the amount of sleep a person needs is age dependent. New born babies tend to sleep for an average of 16–18 hours per day, which decreases to about 13–14 hours after one year. Adolescents tend to require more sleep than adults, possibly due to the physiological changes that are happening in the body during this period. As the person reaches adulthood, they tend to sleep 7–8 hours per day. Older adults tend to sleep roughly 6–7 hours per day, but take more frequent naps throughout the day.

Sleep architecture in humans is divided mainly into non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep. We typically pass through four stages of NREM sleep before beginning REM sleep. In total, NREM sleep accounts for about 75–80% of total sleep in an average adult. This process is cyclical and during a single night we may experience four or five recurring cycles of NREM and REM sleep each lasting between 90–110 minutes. Each stage has its own characteristics and importance.

Thus, for a clearer understanding; this article is come to give a brief overview about the normal sleep, physiological processes involved in its regulation, its architecture, and the possible functions that sleep may serve. It also describes the brain circuitry, cell types, and molecules involved in sleep regulation process.

## Introduction

Sleep is a very complicated process that remains as a mystery though many research have been conducted in human and animals to understand its underlying mechanisms. Sleep forms a part of a natural rhythm of life that plays a vital role for our body and brain to function properly. In children and teens, sleep also supports growth and development. In spite of this fact, millions of people still do not get enough sleep and many suffer from sleep deprivation. In a survey conducted by the NSF (1999-2004), the results reported that at least 40 million Americans suffer from over 70 different sleep disorders and 60 percent of adults report having sleep problems a few nights a week or more. Most of those with these problems go undiagnosed and untreated. In addition, more than 40 percent of adults experience daytime sleepiness severe enough to interfere with their daily activities at least a few days each month — with 20 percent reporting problem sleepiness a few days a week or more. Furthermore, 69 percent of children experience one or more sleep problems a few nights or more during a week [1].

Humans need a sufficient amount of sleep to feel alert and refreshed and to avoid falling asleep unintentionally during the waking hours. Everyone's individual sleep needs vary. In general, most healthy adults are built for 16 hours of wakefulness and need an average of 8 hours of sleep a night. However, some individuals are able to function without sleepiness or drowsiness after as little as six hours of sleep. Others can't perform at their peak unless they've slept ten hours. Interestingly, the need for sleep doesn't decline with age but the ability to sleep for six to eight hours at one time may be reduced [2] .

Each year the cost of sleep disorders, sleep deprivation and sleepiness, according to the NCSDR (National Commission on Sleep Disorders Research) is estimated to be $15.9 million in direct costs and $50 to $100 billion a year in indirect and related costs. In another statistics and according to the NHSA (National Highway Safety Administration), falling asleep while driving is responsible for at least 100,000 crashes, 71,000 injuries and 1,550 deaths each year in the United States. Young people in their teens and twenties, who are particularly susceptible to the effects of chronic sleep loss, are involved in more than half of the fall-asleep crashes on the nation's highways each year. Sleep loss also interferes with the learning of young people in schools [1].

Thus, in this article we tried to give a concise overview of different aspects related to the sleep, its importance, stages, and its underlying mechanisms that may help the reader to get a simple and clear idea about importance of the sleep.

## Functions of Sleep

Sleep is very essential for our physical and mental health. It has been reported that during sleep, there are some important processes that take place to support the healthy function of the brain and overall physical health, which are particularly important for children and adolescents. Sleep plays an essential role in the consolidation of memory. It is believed that sleeping and dreaming help in the process of sorting through experiences and memories to isolate and store the specific details of the memory. Additionally, sleeping is thought to help clear out toxins that accumulate in the brain throughout normal daily activities. Beta-amyloid is a protein associated with Alzheimer's disease is an example of one such toxins. During sleep, channels in the brain expand to allow the flow of cerebrospinal fluid to clear the debris, known as the glymphatic system, due to the similarity to the lymphatic system. Sleep is also essential for maintenance of physical health of the body, particularly in the healing and repair of cells, such as those in the cardiovascular system. The processes of growth and development are also intricately involved with sleep. Deep sleep triggers the release of growth-promoting hormones, which boost muscle mass and repair cells and tissues in the body. The immune system also relies on sufficient quantity and quality of sleep and deficiency in sleep is linked to difficulty fighting infection and increased risk of sickness. Finally, sleep is considered as a strong determinant of productivity during the day at work or in studies. People who lack adequate sleep, often take longer time to finish tasks, are more likely to make mistakes and have a slower reaction time [3 ,4].

## Theories of Sleep

There are several prominent theories that appeared in an attempt to explore the brain and identify a purpose for why we sleep. The most common theories are: Inactivity theory, Energy conservation theory, Restoration theory, and the Brain plasticity theory. Here is a brief description for each of those theories: ***Inactivity theory*** is based on the concept of evolutionary pressure where creatures that were inactive at night were less likely to die from the predation of injury in the dark, thus creating an evolutionary and reproductive benefit to be inactive at night[5]. ***Energy conservation theory*** posits that the main function of sleep is to reduce a person's energy demand during part of the day and night when it is least efficient to hunt for food. This theory is supported by the fact that the body has decreased metabolism of up to 10% during sleep[5].The ***Restorative theory*** which states that sleep allows for the body to repair and replete cellular components necessary for biological functions that become depleted throughout an awake day. This is backed by the findings many functions in the body such as muscle repair, tissue growth, protein synthesis, and release of many of the important hormones for growth occur primarily during sleep [Sharma]. Finally, we have the ***Brain plasticity theory*** that says sleep is necessary for neural reorganization and growth of the brain’s structure and function. It is clear that sleep plays a role in the development of the brain in infants and children and explains why it is necessary that infants sleep upwards of 14 hours per day[5].

Those theories are not exhaustive or all-inclusive of the prevalent ideas; rather, they serve to frame the concept that we do not fully understand sleep yet. It is more accepted that no single theory explains it all, and a combination of these ideas is more likely to hold the key to sleep.

## Mechanism of Sleep

There are two centers in the brain in which the generation and maintenance of sleep-wakefulness states take place: the arousal (wakefulness) and sleep centers. As shown in figure 1, the cortical activation supported by an extensive network of subcortical structures and pathways are necessary to maintain wakefulness state. The releasing of neurochemical is responsible for activation this center and keeping wakefulness state. Major Neurochemicals of this arousal system include excitatory norepinephrine arising from the locus ceruleus (LC), serotonin from the midline raphe nuclei, histamine from the tuberomammillary nucleus, dopamine from the ventral periacqueductal gray matter, acetylcholine from the pedunculopontine tegmentum, and the laterodorsal tegmentum of the pons and orexin from the perifornical area. On the other hand, generation and maintenance of sleep require suppression of activity in the ascending arousal systems. This is accomplished by inhibitory neurons of the ventrolateral preoptic area (figure1), which remain active throughout sleep. The molecular “triggers” that activate the VLPO and initiate sleep onset have not been fully defined, but a substantial body of evidence points to extracellular adenosine as a candidate. Adenosine accumulates in basal forebrain during wakefulness and diminishes with ongoing sleep [6,7]. Adenosine receptors are expressed in the VLPO and adenosine activates VLPO neurons in vivo[8], making it a reasonable candidate for the “sleep switch”. It worth mentioning that caffeine and theophylline are potent adenosine receptor antagonists, which may form the basis for their well-known alerting effects. Despite this evidence, it is almost certain that other molecules also play important signaling roles controlling the initiation and maintenance of sleep. The monoaminergic arousal centers project to the VLPO and may serve to inhibit its activity [6,9]. This creates the concept of “flip-flop” control of behavioral state, in which, at any given time, activity of either arousal producing or sleep-producing neurons dominates and suppresses the other [10]. Homeostasis process and circadian rhythm are responsible for regulating this flip-flop system of sleep-wake states.

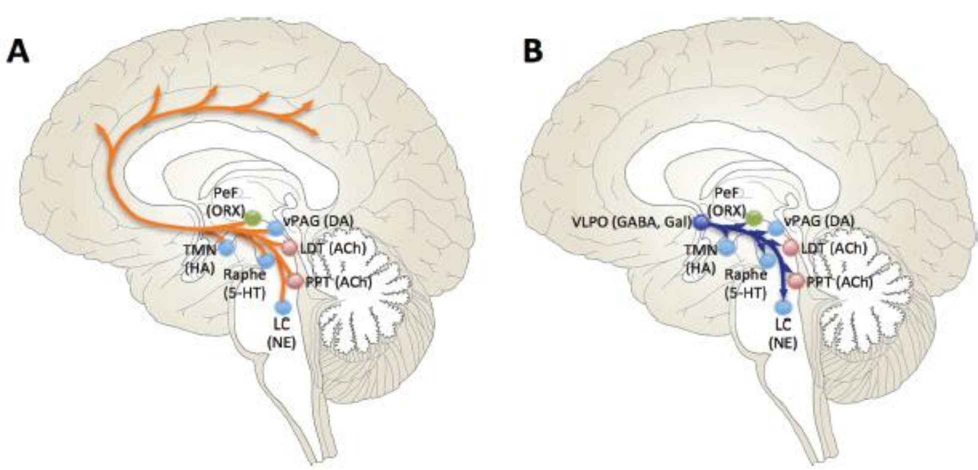


**Figure 1:** A schematic drawing showing the neurochemical and pathways of arousal center (A) and sleep promoting center (B) [David and Farabi etal.].

## Sleep-Wake Regulation

The timing and structure of the sleep-wake cycle are mainly determined by the interaction of homeostatic and circadian drives. The homeostatic drive depends on the amount of preceding wakefulness: the longer the time spent awake, the greater the propensity to sleep. Circadian drive on the other hand is independent of the amount of preceding sleep or wakefulness, it promotes sleep during the night and wakefulness during the daylight hours [11,12]. These two separate biological processes interact and balance each other to regulate the sleep-wake cycle. Sleep homeostasis is characterized by an increase in sleep pressure following sleep deprivation wakefulness (i.e. one is sleepier the longer one is awake). When the homeostatic sleep drive is at its greatest distance from the circadian drive for arousal the "sleep-gate" opens (Figure 2). The need for sleep decreases as sleep accumulates. The homeostatic regulation of sleep compensates for a previous sleep loss and adjusts the sleep duration and sleep depth to match the physiological need for sleep in healthy individuals. A prolonged waking period will be followed by a prolonged period of sleep, called recovery sleep. This provides a possibility to stay awake during certain periods when necessary and then regain the sleep loss when possible [13].

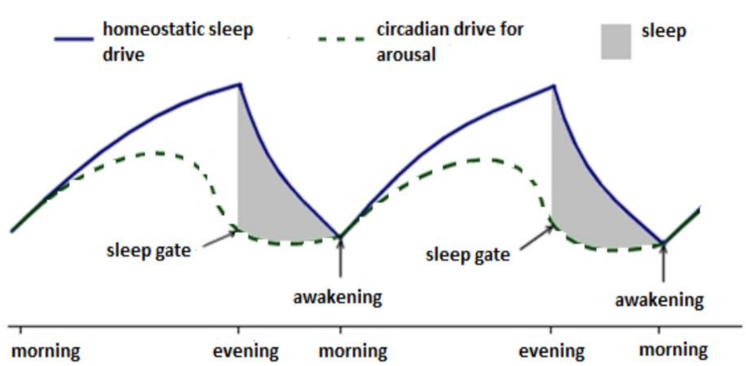


**Figure 2:** Sleep-wake regulation: interaction between the homeostatic sleep drive and the circadian drive for arousal [Angelhoff]

## Stages of Sleep

Natural sleep is divided into two distinctive states: non-rapid eye movement (NREM) and rapid eye movement (REM) sleep. NREM sleep is then further divided into 4 stages where stage 1 is the lightest and stage 4 the deepest level of sleep. REM sleep is divided into phasic and tonic phases. The two distinctive states follow a regular pattern called a sleep cycle which, in an adult, lasts about 90 min and comprises a period of NREM sleep followed by REM sleep. The cycles may be separated by a period of wakefulness and are repeated 3–6 times each night and are typically displayed as a hypnogram (figure 3). The majority of deep (stage 4) NREM sleep occurs in the first and second cycles. As the night progresses, the proportion of REM sleep in a cycle increases and the NREM element is of lighter stage 2 sleep [12,14].

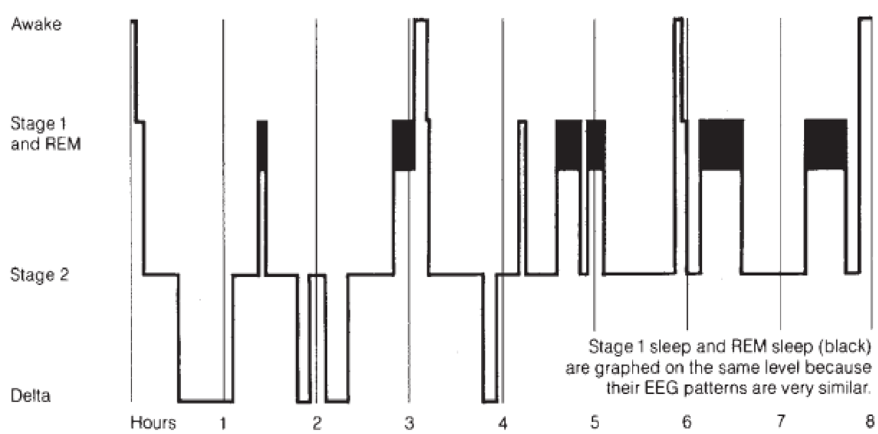


**Figure 3:** A typical hypnogram in adult.

## Sleep Stages Classification using EEG and EMG

EEG frequency bands provide essential information of how brain regions, cells, and molecules regulate wakefulness, sleep states, and display dysfunction due to related pathologies. In this section we are going to explain each EEG band that helps in the classification of sleep stages. The EEG pattern of drowsy wakefulness consists of low-voltage rhythmic alpha activity (8–13 cycles per second (Hz)). In stage 1 of

NREM sleep, the low-voltage mixed frequency theta waves (4–8 Hz) replace alpha rhythm of wakefulness. The muscle activity is highest during wakefulness and diminishes as sleep approaches. Stage 1 is viewed as a "shallow" sleep, during which an individual can be easily aroused, see figure 4. With transition to stage 2, EEG patterns termed sleep spindles and K complexes appear on the EEG. Sleep spindles are 12-14Hz synchronized EEG waveforms with duration of 1.5 seconds. Sleep spindle waves arise as a result of synchronization of groups of thalamic neurons by the GABAergic thalamic spindle pacemaker. The origin of K complexes is unknown. With the onset of stage 2, the arousal threshold increases, and a more intense stimulus is needed to arouse a sleeper. Stages 3 and 4 of NREM sleep are defined by synchronized high-amplitude (>75 μV) and slow (0.5–2 Hz) delta wave EEG pattern. Stages 3 and 4 collectively are referred as deep sleep, delta sleep, or slow-wave sleep. By definition, delta waves account for 20% to 50% of EEG activity during stage 3 and greater than 50% of EEG activity during stage 4 of sleep. The EMG tracks continued muscle tone decline as NREM sleep "deepens" from stages 1 to 4 [14, 12,15].

The cortical EEG pattern of REM sleep is characterized by low voltage and fast frequencies (alpha or 8–13 Hz). This EEG pattern is referred as activated or desynchronized and also is seen in the state of relaxed wakefulness (with eyes closed). Activated refers to an active mind (dreams) and the EEG pattern characteristic of wakefulness. Paradoxically, individuals in REM sleep, although activated, are behaviorally less responsive than during the wake state. Desynchronized refers to the random-appearing wave pattern seen on the REM sleep EEG, which is contrasted with the synchronized uniform wave pattern seen on the NREM sleep EEG. REM sleep can be subdivided further into two stages: tonic and phasic. The tonic stage is continuous and shows muscle atonia and desynchronized EEG as two main features. Superimposed on the tonic stage of REM are intermittent phasic events, which include bursts of rapid eye movements and irregularities of respiration and heart rate [12].

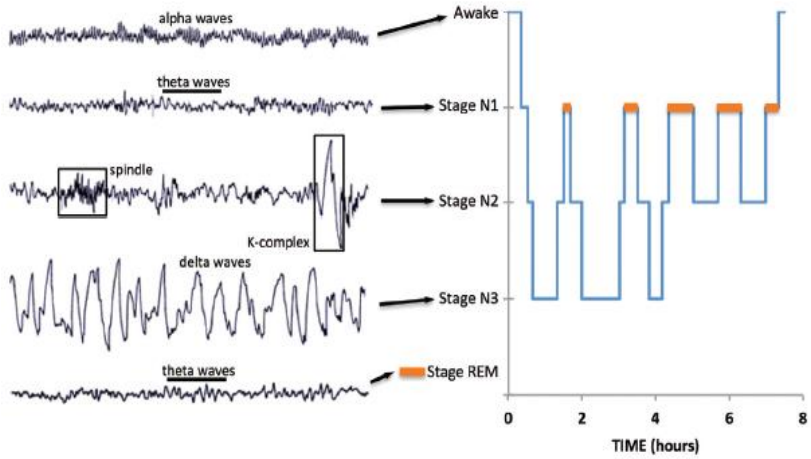


**Figure 4:** EEG bands during sleep/wake stages (left) and typical hypnogram in an adult.

## Sleeping and Dreaming

REM and deep sleep stages are well-known for their role in memory consolidation. Since the middle 1950s, when REM sleep was identified, sleep research has focused on understanding the physiology of dreams and how they happen. Most dreams (about 80%) occur during REM sleep stage; the remainder occur during NREM sleep. REM sleep dreams are more complex, have more emotional valence, can be bizarre, and are easier to recall. NREM sleep dreams are more logical and realistic, but more difficult to recall possibly because awakening from NREM sleep leaves a person feeling more confused and disoriented than awakening from REM sleep. The most accepted theory about dreams is that during REM sleep, neuronal signals originating from the brainstem are transmitted to the cerebral hemispheres and stimulate the cortical association areas to produce images that compose dreams [16]. Neuroscientists still working on many experiments that are conducting on human and animals to get a clearer explanation of the relationship between sleep and dreaming.

## Effect of Age on Sleep

Age is considered as the strongest factor that affects sleep architecture and its stages distribution through the night. The sleep pattern of newborn infants is different from that of adults. Researches have shown that during the first year of life, infants sleep twice as much as adults and, in contrast to adults, enter sleep through REM. During the first year of life, REM sleep occupies about 50% of the total sleep time; this percentage occupied by REM sleep decreases to adult levels of 20% to 25% by age 3 years and remains at that level until old age. As we said earlier in this article that NREM-REM cycles, controlled by the circadian process, are present at birth, but the 50 to 60minute cycle periods in newborns are shorter than the approximately 90 minute periods in adults. Slow wave sleep (deep sleep) is not present at birth, but develops by age 2 to 6 months. The amount of slow-wave sleep steadily declines from maximal levels in the young to almost nonexistent a sleep, sleep changes in the elderly include sleep fragmentation, increased percentage of stage 1 sleep, and decreased ability to maintain continuous sleep at night and wakefulness during the day. Contrary to commonly held beliefs, the need to sleep does not decrease with the advancing age; what changes in the elderly is the ability to maintain sleep [12]. This subject needs more investigation, thus the accurate understanding of sleep quality is essential in understanding and supporting healthy ageing across different stages of life.

## Conclusions

This article highlights different aspects of sleep. To summarize, sleep is an active process that is regulated by homeostatic process and circadian rhythm. Sleep has a typical architecture characterized by a rhythmic alternation between NREM and REM stages, and the transitions among sleep/wake states are orchestrated by a well-defined subcortical network of brain structures. Those stages can be classified based on some features derived from EEG and EMG data. Sleep deprivation can affect the: function of immunity system, regulation of the physiological processes such as glucose level, blood pressure, and body temperature, memory consolidation, and mood**.** Knowing that sleep deprivation is a serious problem that is growing year after year and threating the physical and mental health of people, it is important to raise the awareness of sleep importance and work on enhancing its stages.

## Recommendations

Although the amount of sleep the individual gets each night is very important, one must know that there are other aspects of the sleep that may contribute to the overall health and well-being. Good sleep quality is also essential. Signs of poor sleep quality include not feeling rested even after getting enough sleep, repeatedly waking up during the night, and experiencing symptoms of sleep disorders (such as snoring or gasping for air). Improving sleep quality may be helped by better sleep habits or being diagnosed and treated for any sleep disorder you may have. There are some tips that people must be aware about them to improve their sleep's quality such as: going to sleep at the same time each night, and getting up at the same time each morning, avoid taking naps after 3 p.m., and don't nap longer than 20 minutes, stay away from caffeine and alcohol late in the day, don't eat a heavy meal late in the day, and turn off the TV and other screens at least an hour before bedtime.

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