

# The physiology of sleep for clinicians

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## Abstract

The quest to learn about the need, organization and the functions of sleep has led to basic understanding of physiology of human sleep. Just like wakefulness, different stages of sleep exert unique influence on organ systems of the body. The amount and quality of sleep seems to be in part, controlled by the competing endogenous rhythms. The autonomic system demonstrates characteristic changes with each sleep cycle of non rapid eye movement and rapid eye movement sleep. Cardiovascular physiology provides evidence of "rest and relaxation" during most of the sleep. While behavioral and wakefulness drive to breathe ceases during sleep, respiratory mechanics and ventilatory responses change predictably. Sleep influences most hormone secretion and their actions. Thermoregulation is linked to the sleep wake cycle. Thorough understanding of sleep physiology not only facilitates the approach to diagnosis and management of clinical sleep disorders but also serves to stimulate inquiry, discovery and innovation.

Sleep is a reversible state of behavioral quietness and lack of responsiveness to normal stimuli. It is opposite to the state of the wakefulness where there is an awareness of the surrounding environment and normal responsiveness to stimuli is present. During sleep many physiologic, metabolic and neurobehavioral functions are ongoing and are organized within highly complex relationships. There are three well defined states of being; the wakefulness, non-rapid eye movement (NREM) sleep and the rapid eye movement (REM) sleep. Wakefulness occurs for approximately sixteen hours a day while sleep is about eight hours.<sup>1,2</sup> The NREM sleep is about 75% of the total sleep time where as REM is 25%. NREM sleep is further divided in to N1, N2 and N3 sleep. The REM sleep is of tonic and phasic types.

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NREM and REM sleep cycle every 90 to 120 minutes for four to six cycles every night.

Despite multiple hypothetical theories there is a lack of a unifying theory of the function of sleep.<sup>3,4</sup> According to the restorative theory the sleep is essential for the tissue and brain restoration. This theory is supported by the release of the growth hormone during sleep. The energy conservation theory is based on the fact that animals with higher metabolic rate need longer sleep. During sleep there is reduction in energy expenditure and oxygen consumption in the brain as well as an increase in the levels of energy substrate like adenosine triphosphate. The adaptation theory revolves around the ability of the subject to adjust to the changing environment to survive.<sup>5</sup> During the darkness sleep provides for the avoiding exposure to predators. The memory consolidation theory is supported by many established facts of retention of information learned during the wakefulness. Sleep processes participate in the consolidation of the memory. In this process the memory traces are reactivated, analyzed and incorporated in to long term memory. The neural plasticity theory

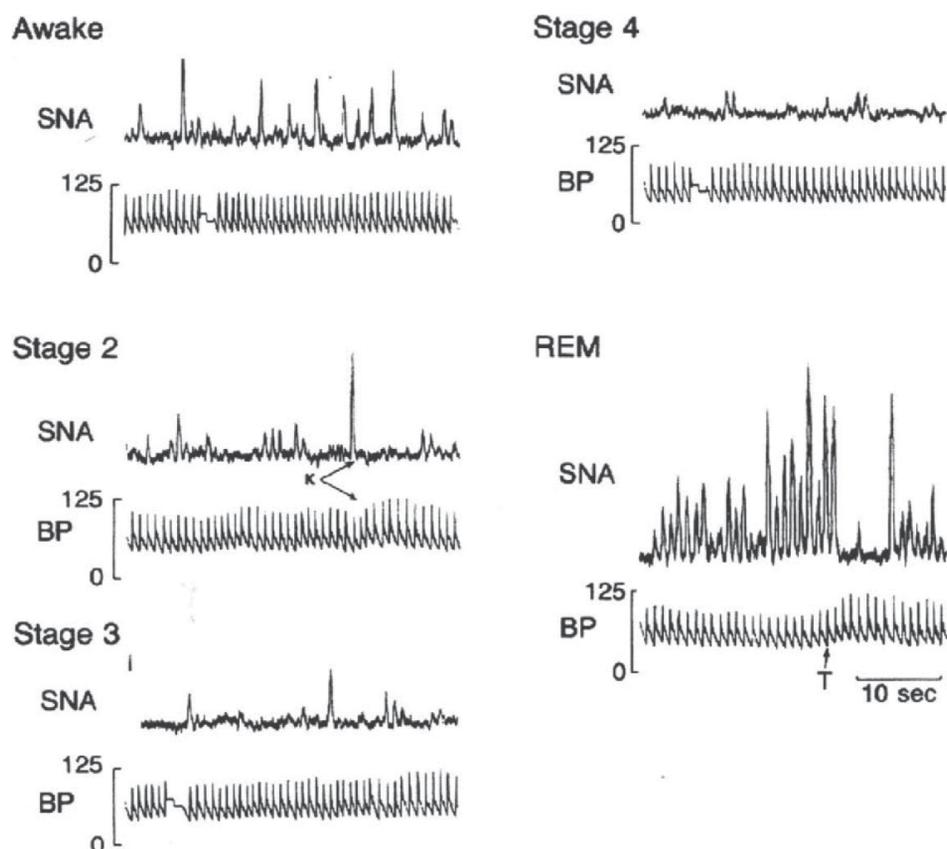
relates to the synaptic integrity and suggests that sleep maintains motor and non-motor circuits. The thermoregulatory theory is supported by the lack of thermoregulation with sleep deprivation and its maintenance during normal sleep. Experimental data supports that sleep may be regulatory for the immune function in the body. Deterioration of the immune function is well documented due to sleep deprivation.<sup>6</sup>

In the two-process model, the sleep is controlled by a balance between an independent and intrinsic circadian rhythm (process C) that is innate, temperature compensated and not-learned process. Circadian rhythms are generated by the biologic clock and they can be synchronized or entrained by external time cues, especially the daily light-dark cycles. The second is homeostatic process (process S) that depends on the sleep wake cycle of the individual. The homeostatic sleep drive increases with increasing time of wakefulness. These two processes achieve sleep homeostasis despite two wake maintenance zones and two sleep propensity zones related

to circadian drive and sleep load related to homeostatic process.<sup>7</sup>

Sleep has its own unique effects on the body systems. It seems to influence autonomic changes involving the cardiovascular, respiratory and thermoregulatory systems. A combination of increased parasympathetic activity in non-REM and tonic REM sleep and intermittent sympathetic activity in REM sleep results in these changes. Transient bursts of sympathetic activity occur during the arousal from the non-REM sleep.

The cardiovascular physiologic changes during the sleep are a reduction in the heart rate, cardiac output and the blood pressure.<sup>8,9</sup> The decrease in heart rate seems to be due to increased parasympathetic activity through an increase in the vagal activity. In general, the systemic vascular resistance and the stroke volume remain unchanged during sleep. Approximately ten percent reduction in blood pressure is known as nocturnal dip. The blood flow to cutaneous, muscular and mesenteric



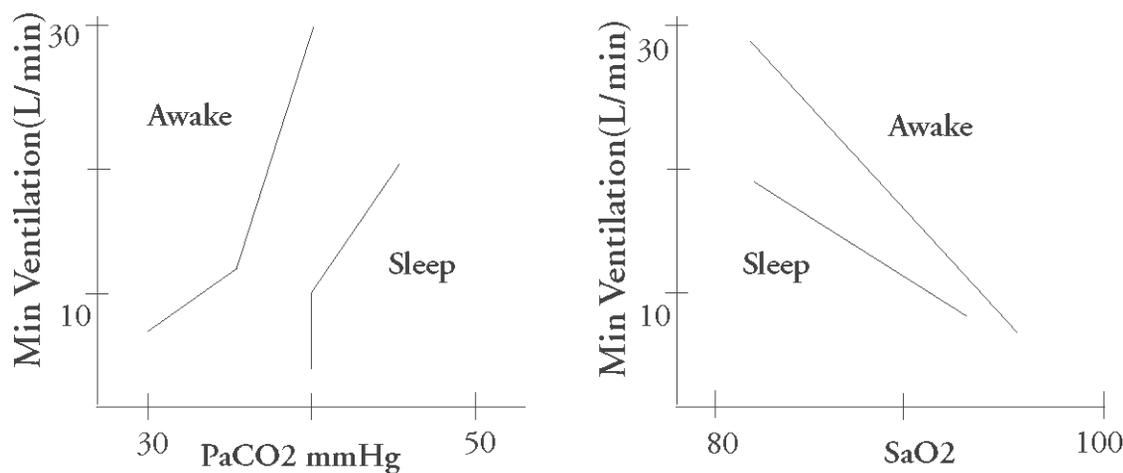
Recordings of sympathetic nerve (SNA) and blood pressure activity in normal person while awake and while in different stages of sleep. Reduction in SNA activity and blood pressure variability is noted during non-rapid eye movement sleep. (Stage 4 is now scored as N3 per 2007 scoring guidelines). Significant increase in both parameters present in Rapid eye movement sleep.<sup>5</sup>

vascular beds changes minimally. During REM sleep however, the mesenteric and renal blood flow increases while vasoconstriction occurs in cutaneous and muscular vascular beds. These sleep stage related changes occur throughout the night. The cerebral blood flow, cerebral oxygen consumption and glucose utilization are all reduced during the non-REM sleep but are increased during the REM sleep. Pulmonary arterial blood pressure increases only slightly in the sleep.

As opposed to both the metabolic and voluntary drive to breath, only metabolic system drives the ventilation during the sleep. Periods of central apneas may occur at the sleep onset. There is a reduction in the upper airway muscle tone and increase in the resistance to the air flow. The airway resistance is highest in REM sleep. The alveolar ventilation and the minute ventilation are both decreased during the sleep due mainly to reduction in the tidal volumes. The functional residual capacity declines by ten percent during sleep. While breathing is more regular in non-REM sleep, it becomes irregular during the REM sleep. The hypercapnic and hypoxic ventilatory responses are relatively blunted during the sleep. There is a mild decrease in the partial pressure of oxygen and increase in the partial pressure of carbon-dioxide in the blood. The oxygen saturation generally decreases less than two percent during sleep. Both the oxygen consumption and the carbon di oxide production are reduced. The cough reflex is attenuated both in non-REM and REM sleep.<sup>10</sup>

Hormone secretion is directly linked to specific sleep stages.<sup>11,12</sup> The growth hormone and prolactin are released during the slow wave sleep (N3). The secretion of the growth hormone typically peaks approximately 90 minutes after the sleep onset. The cortisol secretion is linked to the endogenous circadian rhythm. Cortisol secretion is reduced during the sleep. The increasing levels of the cortisol occur in the early morning. Many studies have shown the cortisol levels to be the same during normal sleep and sleep restriction suggesting its secretion to be independent of sleep. In men the testosterone levels are highest during the sleep. Thyroid stimulating hormone secretion is inhibited by the sleep. It peaks in the evening and also increases during the awakenings and with sleep deprivation. The melatonin levels increase in the evening, peak in the early morning and then gradually decline during the daytime. Insulin levels decline during the sleep. Sleep deprivation may cause insulin resistance. The Aldosterone levels peak just before awakening in the early morning. The rennin activity is lowest during the REM sleep. Antidiuretic hormone does not show any relationship to sleep. There is no consistent relationship noted between sleep and the gonadotropin hormone, luteinizing hormone and follicle stimulating hormone.

The urinary volume decreases during the sleep due to reduced glomerular filtration, altered rennin release and increased water reabsorption. There is penile and clitoral tumescence present during the REM sleep.



#### Ventilatory response to high Co2 and low O2

The ventilatory response hypercapnia and hypoxia declines during sleep. The response is much less in REM sleep than in the NREM sleep

The saliva production, swallowing and esophageal motility is suppressed during sleep. There is prolonged mucosal acid contact as a result and there is prolonged acid clearance. The migratory motor complex, a special pattern of motor activity shows a circadian rhythm with its slowest velocity during the sleep. Basal gastric acid production peaks between 10 pm and 2 am and is lowest between 5 pm and 11 am. The lower esophageal sphincter tone does not show any circadian variation. The colonic motility index is inhibited during the sleep followed by a marked increase upon awakening.<sup>13,14</sup>

Body temperature is linked to the sleep wake cycle but is independent of the circadian rhythm. The core body temperature peaks in the late afternoon and falls at the sleep onset. It is lowest early in the morning between 4 am and 5 am. Thermoregulation is absent during REM sleep.<sup>15</sup> Metabolism decreases during the non-REM sleep but is equal to or higher during the REM sleep.

There is an increase in parasympathetic activity both in non-REM and REM sleep. The sympathetic activity is decreased in sleep. During the phasic REM sleep there is a sharp increase in the sympathetic activity in skin and muscle vascular beds. The tonic parasympathetic activity causes constriction of the pupil in non-REM and tonic REM sleep. The central inhibition of the parasympathetic flow to the iris causes dilatation of the pupil.

This article summarizes the major physiologic processes during sleep across the functions of the organ systems of the body. It is important to completely understand the normal physiology of sleep before attempting to learn the patho-physiologic mechanisms underlying the sleep disorders. The knowledge of basic physiological processes provides a solid foundation to interpret the deviation from the normal, its impact on human health and effective management of the clinical disorders.

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