Circadian Rhythm & Its Effect on Health

Prof. Dr. Faisal Abdullatif Alnaser, FPC, FRCGP, MICGP, FPH, FAM(USA), PhD

Professor of Family Medicine
Faculty, Dept. of Primary Care & Public Health, Imperial College, London
General Secretary and Treasurer, International Society for the History of Islamic Medicine
Chairman, Home Health Care Centre, Bahrain

Email: faisal.alnasir@gmail.com

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Research Article

Abstract

Circadian Rhythm (CR), which is the interchange between day and night, has a vital role in the health of all living creatures including plants. It is a biological process that echoes an internal clock in the body oscillating during the whole 24 hours of the day. Within that time, it fluctuates to control the sleep period that alternates with wakefulness at regular intervals. There is a complex interaction between sleep and all parts of the human body. A good night's sleep influences CR and is essential for the body organs and cells' efficient physiological function. Industrial development, modernization, and many other illnesses are all causes for the disturbance of the CR. Such disruption may lead to several dangerous health problems like; cerebral problems, cardiovascular diseases, pulmonary embolism, metabolic syndromes, infections, gastrointestinal issues, menstrual irregularities, mental disorders, and psychiatric illnesses. Besides, CR disruption has a carcinogenic effect on various organs. In this review, we highlight the functional importance of CR and the health consequences of its disruption.

Keywords: Day, night, Circadian Rhythm, Health effects, Biological Clock, SCN, Dawn Phenomenon

1. Introduction

Why is there dark and light, and night and days? Why life is not consistent with either days or nights? Furthermore, for what reason there should be an alternation between them? And do such alternations have any effect on the health of living creatures, in particular, human beings? There must be logical and vital answers to all those questions.

The enlightening of the day and the darkness of the night are just the normal earth's division into periods of movement, action, activity, rest, recovery, and stillness. For that, scientists have extensively studied the rhythmic changes of dark and light to find their importance and their significant impact on health. The importance of the interchange of the day and night was highlighted in 92 verses of the Holy Quran fourteen centuries ago. Versus 12 of Surat Al-Isra stated, "And we have made the night and day two signs, and we erased the sign of the night and made the sign of the day visible that you may seek bounty from your Lord." [1]
From birth and till death, the cells and organs of the human body have unique functions to do. And many of these functions are influenced by the cyclic phase of the day and night. For efficient performance of all body organs, except the heart, there is a critical need for pause and rest, to recharge such organs. That can only happen when there is a healthy, effective, and sufficient amount of sleep. Good sleep is the only one made on a daily basis and mainly during the darkness of the night. On the next day of such adequate sleep at night, the body becomes relaxed, comfortable, and energetic. In addition, the mood is boosted, the behavior is sedated, and the person feels much better. Because the brain will be more relaxed and restored after such a good night's sleep, it will be able to function better, be more productive, could concentrate, and memorize new learning materials more efficiently. The memory consolidation of the brain occurs mainly during slow-wave sleep when growth hormone is secreted. As the brain reconsolidates, all of the gathered information during the day that enriches memory will be quickly retrieved whenever it is needed.

Since there is a complex interaction between sleep and all parts of the human body, sufficient and healthy sleep is not a luxury but is a necessity. It is also a vital physiological process for the efficient function of the body's organs and cells leading to a healthy lifestyle living.

2. Characteristics of Circadian Rhythm
The oscillation of day and night into cycles is called Circadian Rhythm (CR), which is not only found in humans, but almost all living things like animals, plants, and many tiny microbes. CR is a biological process that echoes an internal clock in the body oscillating during the whole day. It fluctuates within the 24 hours of the day to control the alternation between the sleep and wakefulness period at regular intervals (also known as the sleep/wake cycle). CR helps the human body adjust and change its energy requirement depending on the changes occurring in the external environment. In explaining that process, Foster and Wulff said, "CR helps to adjust the energy requirement and its use by the body. Due to various activities that are done mostly during the day, the energy requirements in that period are increased while decreasing during the night." [2]

Since the body's energy utilization is in constant change, it has to be controlled and adjusted to the dark and light cycle of the night and day to ensure the efficient performance of the body's biological system. The lowest energy requirements happen mainly during the middle of the night.[3] For that, a good night's sleep is required for the CR to work at its best. The mechanism of CR, although complex, is more or less similar to an alarm clock, warning the body and its organs about the changes that happen in the external environment during the day and night. Hence, the CR response is coordinated to the external environment.[4] Such coordination is set up by a biological clock (also called the internal master clock) that triggers the CR and regulates its timing. The biological clock of the human is situated at the suprachiasmatic nucleus (SCN) of the brain's hypothalamus and is made up of about 20,000 nerve cells (neurons). The primary function of the SCN is triggered by light stimuli, leading to the adaptation of the body to environmental changes. Simultaneously, the biological clock synchronizes the body's biological process, physiological functions, and behavioral responses with external environmental changes. There is a direct relationship between such synchronization and many bodily hormones (which will either stimulate or inhibit the secretion of these hormones) affecting the body's mental, physical, and psychological functions. Such stimulations are reflected in eating habits, digestion, body temperature, and other critical bodily functions. Moreover, many physiological processes that are controlled and adjusted by the CR will be affected, leading to fluctuations of body temperature, secretion of hormones (like glucocorticoid), immune regulation, cytokine release, and cell cycle progression.[4] The neurohumoral processes and environmental stimuli trigger the body organs to harmonize their function, operations, and activities.[5] In addition to the sleep and wakefulness cycle, other factors influence the CR, such as the body and environmental temperature, alertness, food intake,[6] the oxidative or hypoxic stress stimuli, and mechanical factors.[5,7]
3. Disturbance of Circadian Rhythm
CR despite being complex, is a highly sensitive system, making its functions liable to be disrupted by many factors. The dysfunction is mainly the result of four main elements: mutations in the genes responsible for circadian oscillation; conditions that prevent light from entering the body (such as blindness or age-related reduction of photoreception); inadequate artificial lighting (too dim and low in short wavelengths); defective nerve pathway from the retina to SCN, or any pathology that contribute to dysfunction of the SCN. The consequence will be a disturbance of sleep and organs' malfunction. Nonetheless, one of the most important external factors that could disturb the CR is related to the so-called modernization and industrialization (with shift work). Both have lead to behavioral changes reflected in irregular night sleep. In addition, disturbance of CR started to happen when artificial light was introduced to the public, making people stay awake late in the night. Those who opt to stay awake late in the night, including shift workers, would disturb their CR. The almighty God has created the human body with an organized and calibrated cellular and organic function. For that, human bodies need to rest at certain hours of the day so that their cells and organs properly operate for healthy living during wakefulness. Other factors leading to disturbed CR are pregnancy, jetlag, stimulant medications, addiction drugs, mental, medical, and psychiatric problems, including Alzheimer's or Parkinson's disease.

4. Melatonin and Circadian Rhythm
Alteration of the day and night cycle is also controlled by Melatonin secretion, which is an important hormone that plays a significant role in initiating and maintaining sleep. Any reduction in its blood level will lead to sleep disturbance. Melatonin, although produced mainly from the pineal glands that lie in between the two halves of the brain, there is also an extra-pineal source from the gastrointestinal system. Once secreted into the bloodstream and cerebrospinal fluid, it reaches its peak level during the night. Blue light and light rays passing through the retina to the SCN of the Brain during the daytime suppress Melatonin secretion, leading to disturbed night sleep. Melatonin secretion has also a seasonal rhythm; its level is highest in autumn and winter (when nights are longer) and lower in the spring and summer. Moreover, Melatonin blood level was found to be reduced in people working at night, obese, in Dementia, mood disorders, severe pain, cancer, type2 diabetes, and in the elderly (aging causes diminished sleep duration at night). People who complain of disturbed night sleep are at more risk of clinical impairments of the metabolic and physiological processes of the body, increasing the probability of morbidity. They are susceptible to develop metabolic syndromes (obesity, hypertension, hyperglycemia, and dyslipidemia). In highlighting that point, Octavian CL stated that the decrease in sleep duration in the US has occurred over the same period of increased prevalence of metabolic disease.

5. Illnesses that are related to diurnal variation
As CR is essential for almost all bodily vital processes, several dangerous health problems could be associated with its disturbance. When CR cannot synchronize itself with the changes in the external environment, health problems usually start to occur. Furthermore, numerous reports indicated that several health events are more prone to happen in the early morning hours of the day than at other times. During those hours impairment happens in several physiological functions like autoregulation, cerebrovascular reactivity, nervous system function, coagulability, heart rate, platelet agreeability, the concentration of blood catecholamine, and cerebral blood flow (due to an increase in the blood pressure). Due to the stated changes and the triggered inflammatory pathways, the risk increases in the early morning to get cerebrovascular events and other complications such as angina pectoris and myocardial ischemia. Sudden cardiac death, pulmonary embolism, limb ischemia, and rupture of aortic aneurysm are also associated with CR's disturbance. Studies indicated that between 6 AM and noon, there is a 40% higher risk of acquiring heart attack, 29% increased risk of cardiac death, and 49% increased risk of stroke. Knutson et al. found that the risk of a
fatal heart attack increases by 45% in individuals who chronically sleep less than 5 hours per night.\textsuperscript{[24]} Hypertension is also associated with sleep loss. A fundamental question is whether these events are triggered due to the CR variation in responses to the circulatory function (or exercise) or are related to inevitable hormonal fluctuation during the 24 hours of the day. Moreover, CR disruption in diabetic and non-diabetic individuals may lead to a condition called the Dawn Phenomenon. Dawn Phenomenon is defined as the periodic incidence of elevated blood glucose occurring around wakening hours (between 4-8 AM).\textsuperscript{[15,16]} Although the exact underlying causes are still unclear, it is primarily due to changes in the hormonal level related to the diurnal variation. These hormones, including adrenaline and cortisol, are secreted more in the early morning, leading to an increase in their concentration in the blood circulation. In normal circumstances, the increased hormonal production happens in response to prepare the body for performances during that day. In addition, both the Glucagon and Growth hormones, promote glucose release into the blood circulation leading to hyperglycemia in the early morning. Therefore, the Dawn phenomenon may negatively affect diabetic patients (due to the increased blood sugar that is associated with worsening HbA1c levels). Ultimately, the Dawn phenomenon challenges diabetic control leading to ketoacidosis and damage to organs, nerves, and blood vessels.

6. Problems related to disturbed Circadian Rhythm

Studies suggest that metabolic processes and sleep are interrelated with the biological rhythms through a complex interaction in the molecular pathways.\textsuperscript{[18]} A positive correlation between increased body weight in children and reduced sleep duration has been documented.\textsuperscript{[21]} Decreased sleep usually enhances the hunger sensation. It deters the hormone's signals responsible for satiety (reducing circulating leptin levels), leading to polyphagia and reduced glucose and lipid metabolism.\textsuperscript{[22]} Disturbed sleep affects the sleep-wakens cycle and the food eating or abstaining behavior and ultimately altering the physiological process of the produced energy (whether utilized or stored). Such increased food intake (in particular fatty food) leads to increased body weight.

Other conditions associated with disruption of the CR are; infections, gastrointestinal problems, menstrual irregularities, increased risk of accidents,\textsuperscript{[25]} health problems related to hormonal changes,\textsuperscript{[17,26]} Mental disorders, and psychiatric illnesses such as bipolar disorders schizophrenia, and Alzheimer's disease.\textsuperscript{[27]} Studies have found that regular CR and regular sleep (concerning its duration, quality, and time) help in preventing or slowing down Dementia.\textsuperscript{[28]} Epidemiological data from developed countries reported that despite modernization and advancement in the investigation and screening procedures, CR disruption has a carcinogenic effect and may increase the incidence of colon and breast cancer.\textsuperscript{[29-36]} Breast cancer was related to decreased melatonin levels. The reduced concentration of blood Melatonin leads to increased concentration of androgens like estrogen and progesterone.\textsuperscript{[37]} Besides, the stimulatory effect of the secreted estrogen on the growth of mammary cells leading to an increase in cells' turnover, thereby increasing the chance for replication errors.

Melatonin hormone has also protective characteristics; first, it is a potent free radical scavenger because of its antioxidant properties. Second, the inverse relationship between it and the secretion of estrogen and other circulating reproductive hormones. Therefore, a decreased Melatonin level will result in the accumulation of free radicals leading to an increased risk of cellular damage and somatic mutations. It was also found that the risk of Breast cancer, which is related to obesity, may be reduced by Melatonin.\textsuperscript{[38]} Melatonin deficiency in postmenopausal women was found to affect significantly the process of weight gain.\textsuperscript{[23]}

7. Conclusion

Circadian Rhythm is vital for the function of all the body cells and organs and on the individuals' health. Improving sleep quality mainly at night and preserving the Circadian Rhythm will have a positive effect
on the quality of life, in addition, it has a preventative role against many pathological problems that are due to disturbance of Circadian Rhythm.

Conflict of Interest: The author declares no conflict of interest.

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