Transactions on Materials, Biotechnology and Life Sciences
ISSN: 2960-1932, eISSN: 2960-2319 | Volume 3
BLSME 2024

How Light Affects Circadian Rhythm and Mood Regulation

Juan Fu *

Beijing New Oriental Foreign Language School at Yangzhou, Jiangsu, China

* Corresponding author: smcnamara78995@student.napavalley.edu

Abstract. Light is full of the world and illuminates our lives, and scientists believe that light must play a crucial role in affecting humans either positively or negatively including circadian functions and emotion-related behaviors. Through experiments, researchers have revealed the fact that light can affect humans significantly and the principles behind phenomena of light influencing humans both physically and mentally. This essay focuses on how light works in humans' circadian rhythm and mood regulation, and how exactly nocturnal light exposure induces depression-like behaviors. Many research results indicate that natural light can help reset circadian rhythm of humans when the normal circadian rhythm is disturbed by trans meridian travel or working during night. Thus, scientific time of light exposure helps to relieve jet-lag symptoms and allows people to have a healthier mental and physical state. Studies by Fernandez D C et al. and An K. et al. are included in this essay to demonstrate the effects of light on mood. Fernandez D C et al. experimentally confirm that PHb (perihabenular nucleus) is necessary in the circuit of light affecting mood through ipRGC which is the only receptor of light input to influence circadian functions of the brain. Subsequently, An K. et al. conducted a series of experiments on mice to investigate the role of a subcortical pathway regulated by circadian rhythms in modulating mood-related behaviors resulted from nighttime light exposure in mice. The findings provide insights into the mechanisms underlying the impact of nocturnal light on mood regulation and highlight the importance of considering circadian rhythms in understanding the effects of environmental factors on mental health. Overall, these studies allow more scientists to think about how to employ light as therapy as well as development of new anti-depressants based on the research of the ipRGC circuit.

Keywords: circadian rhythm; mood regulation; light; depression.

1. Introduction

Throughout history, the consistent pattern of alternating day and night, caused by regular rotation of the Earth, has persisted without interruption. Over time, creatures on the Earth including human beings have successfully acclimated to this natural cycle, which has become deeply ingrained in their genetic makeup. This is the circadian system that exists in all organisms. If individuals fail to adhere to the guidelines of the circadian rhythm which entails engaging in work activities during daylight hours and obtaining restful sleep during the night, and disrupt the body clock in them, what consequences may arise? Numerous scientists have dedicated years of research to unravel the answers to this question. Ultimately, they have discovered that it is light which significantly impacts individuals both physically and mentally. This is particularly evident when individuals deviate from their circadian rhythm, such as by staying up late to work or engaging in phone-related entertainment. For instance, when people travel across time zones eastward or westward by plane, they commonly encounter the phenomenon known as jet lag. Natural light exposure during daytime has the ability to help relieve the symptoms of jet lag, such as headache, fatigue, and so forth, through adjusting the time and duration of light exposure, and makes people who suffer from jet lag after long flights feel better [1].

Light also has effect on mood regulation. Light pollution is a prevalent issue in contemporary urban areas. The traditional notion of sunset marking the conclusion of the day has been replaced by a widespread exposure to excessive artificial lighting during nighttime. This phenomenon has given rise to significant apprehensions regarding the potential adverse effects on various biological aspects, with a particular focus on mood. Research conducted on both humans and animal models has

provided evidence of the capacity of light to impact behaviors associated with mood, as well as the functioning of brain regions responsible for regulating these behaviors. Initial research has concentrated on examining the direct impact of light. Retinal ganglion cells are essential in transmitting light information to brain regions responsible for visual image processing. In addition, there exists a unique subgroup of retinal ganglion cells which are intrinsically photosensitive (ipRGCs) possessing remarkable ability to directly convert light information. These ipRGCs possess extensive neural connections throughout the brain, allowing them to transmit visual information and modulate diverse physiological processes [2]. Later, research carried out by Fernandez D C et al. revealed that the circadian clock machinery in the PHb (perihabenular nucleus) is selectively disrupted by irregular light/dark cycles through a circuit that is dependent on ipRGCs, and then the mood-related behaviors are directly affected. Under normal lighting conditions, PHb neurons which work in the process of light affecting mood exhibit different excitability during daytime or night [3]. Kai An et al. Conducted several experiments to confirm that it is the ipRGC-dPHb (dorsal perihabenular nucleus)-NAc circuit in the brain to have the direct influence on mood regulation. Moreover, studies show that light from diverse sources with different wavelength and intensity can show different extent to the effect on humans. In particular, the most influential light is blue light [1]. In this essay, the topic how light impacts circadian rhythm and mood regulation will be discussed.

2. Light and circadian system

The term “circadian rhythm” comes from two Latin words, circa and dies (days), which represent approximately one day, with a period close to 24 hours [4]. Circadian rhythms are found in many organisms, such as most bacteria, fungi, plants and animals show very distinct circadian rhythms [5]. As a powerful zeitgeber, light is capable of changing the stage of the internal clock, and is an important factor affecting the circadian rhythm [6]. Numerous studies have identified the disruptive impacts of reduced nighttime lighting on metabolic and mood-related functions in rodents. These findings underscore the potential significance of adequate daytime light exposure in maintaining healthy and regular circadian rhythms [7]. The impact of light on circadian rhythms, particularly with regards to sleep, mood, alertness, and cognition, is a factor in determining their timing and stability [8]. Abnormal light exposure, such as light when working during night or traveling through the meridian, disrupts circadian rhythms and causes circadian dyssynchrony in different systems of the body, ultimately leading to jet lag symptoms and sleep disturbances [9]. At the same time, it can also lead to attention and performance damage, emotional disorders and other problems [10].

Appropriate light exposure allows humans to reset disrupted circadian rhythm such as jet lag led by transmeridian flight, and it depends on the time and duration of exposure, as well as the direction people travel to. For instance, in the approximately 12 hours preceding the minimum core body temperature (CBTmin), exposure to light leads to a delay or backward shift in the circadian system. Conversely, light exposure in the approximately 12 hours following CBTmin results in an advance or forward shift in the circadian system. The most notable changes occur when there is exposure to light during the period of 3-6 hours surrounding CBTmin [1].

3. Light affects sleep

Sleep is a natural behavior that is ubiquitous among almost all organism [11]. During sleep, the body remains still and is less responsive to external stimuli. Sleeping is regulated by the circadian rhythm, and circadian processes can clearly reflect changing trends in sleep and waking activity [12]. The International Commission on Illumination has recently released a position statement titled "Recommending appropriate lighting at appropriate times" which addresses the non-visual effects of light. The commission recommends the implementation of high intensity physiological equivalent lighting during daylight hours as a means to increase alertness, regulate circadian rhythm, and enhance the quality of sleep. Conversely, the commission suggests employing low intensity lighting stimulation during nighttime hours to promote sleep [13]. Some studies have demonstrated the

moderation effect of light on circadian rhythm and sleep quality. Sleep is not only regulated by circadian rhythm, but also by a combination of internal balance and various behavioral factors. The hypothalamic suprachiasmatic nucleus (SCN) and endogenous melatonin of the organism both play a role in regulating sleep. Both are influenced by environmental light and are closely related to sleep. Exposure to night light can lead to delayed circadian rhythms and inhibition of melatonin before bedtime, leading to circadian rhythm disorders and insomnia [14]. A research investigation was conducted to assess the impact of intense light exposure during nighttime on the circadian rhythm and sleep patterns. The findings revealed that exposure to bright light during the night resulted in a delay in the circadian rhythm and an extension of the awakening time for individuals suffering from insomnia [15]. Exposure to night light is the most common way of light affect sleep. From a physiological perspective, the presence of light during nighttime plays a pivotal role in disturbing the operation of the suprachiasmatic nucleus (SCN). Even minimal levels of light at night have the capacity to influence melatonin levels and disturb the circadian rhythm. Based on the circadian rhythm response curve to light, exposure to light during the nighttime period prior to sleep has a greater potential to disrupt the subsequent circadian rhythm compared to light exposure during other periods [16].

As an indicator of the circadian rhythm, the variation in melatonin concentration mirrors the daily fluctuations of sunrise and sunset. It follows a periodic shock pattern, making it a commonly employed measure for assessing the impact of light on the rhythm. A clinical study showed that in a controlled laboratory environment, morning light stimulation can advance the phase of melatonin secretion, thus promoting an earlier sleep time, and nighttime light intensity suppresses melatonin secretion and extends subsequent sleep latency in humans [17]. Another study showed that daytime light stimulation can enhance nocturnal melatonin secretion while enhancing circadian rhythm and reducing sensitivity to night light [18]. Nie et al. (2020) let three subjects work in shifts in an underground enclosed environment for 38 days, using LED dynamic lighting with adjustable color temperature (CCT) and circadian action factor (CAF) to simulate natural light changes [19]. The results of the study revealed that the participants' circadian rhythm exhibited stability and enhancement, accompanied by a notable elevation in the peak concentration of melatonin in their blood. The LED dynamic lighting method that simulates sunlight effectively induces and enhances the circadian rhythm in a closed environment.

4. The effects of light on mood

Light has the ability to influence a range of physiological processes, including mood regulation. It is well-established that light therapy administered during the daytime can effectively alleviate symptoms of depression. However, it has been observed that excessive exposure to light during nighttime hours may be linked to the development of depressive symptoms [20]. The regulation of mood is significantly influenced by light, and the modulation of mood-related behaviors through light requires the involvement of ipRGCs which serve as the sole pathway for light input to regulate brain functions. Research conducted by Fernandez D C et al. was to figure out the effects of light on mood. The researchers concluded that the pHb region of the brain receives input of light from ipRGCs and sends signals to mPFC and NAc. This implies that the pHb serves as a conduit for transmitting light-related information to the aforementioned brain regions, which play a role in modulating behaviors associated with depressive symptoms. In this issue, An et al. further elaborate on the aforementioned groundbreaking research, offering a more comprehensive understanding of the implications of nocturnal illumination and the physiological mechanisms of the perihabenular nucleus (pHb). The authors specifically emphasize the role of ipRGCs and their connection with the pHb and nucleus accumbens (NAc) circuitry in modulating light-induced effects on mood-related behaviors.

5. Nocturnal light induces depression-like behaviors in mice

To find out what are exactly included in the circuit that allows light at night (LAN) to affect mood, An K. et al. have conducted an experiment on mice as an expanded study based on the research done by Fernandez D C et al. before. The mice are kept in a controlled environment where they experience yellow light for half of day followed by darkness for the rest of day. Additionally, they are subjected to a 2-hour pulse of blue light starting 1 hour after the lights are turned off, in order to mimic the effects of artificial light during the night. After being exposed to this light-dark cycle for a period of 3 weeks, the mice displayed regular circadian rhythms. However, they exhibited heightened behaviors commonly associated with depression, such as a decreased preference for sugar and increased immobility during forced swimming tests. These behaviors are believed to be indicative of anhedonia and helplessness, respectively. The effects of the T7 light cycle demonstrate a comparable light-dependent influence to the LAN paradigm. The LAN paradigm entails exposing mice to light at a consistent circadian time each day, enabling researchers to examine the specific effects of nighttime illumination while subjecting the mice to light at various circadian times within the T7 cycle [2]. An K. et al. have demonstrated the indispensability of ipRGC innervation in the pHb region for LAN to influence on depression-related behaviors. Additionally, further research has emphasized the pivotal role played by the circuit ipRGCs-dPHb-NAc in this process. In order to further elucidate the central structure mediating the impact of LAN, it was discovered by the research team that when ipRGCs projected to the pHb and impaired its function, the LAN-induced alterations in emotion-related behaviors of mice were no longer observed. Additionally, optogenetic activation of pHb projection by ipRGCs also induced depression-like manifestations in mice. These findings unequivocally confirm that pHb serves as a crucial hub mediating LAN effects. Subsequent investigations revealed that dorsal pHb (dpHb) projects onto nucleus accumbens (NAc), ventral pHb projects onto NAc, and dPHb projects onto NAc. Furthermore, vpHb is projected into medial prefrontal cortex (mPFC). NAc is involved in the processing of rewards, whereas mPFC is linked to the regulation of emotions and higher cognitive processes. By selectively inhibiting pHb input to mPFC and NAc using AAV viral tools, it was confirmed that only inhibition of dpHb-NAc projection affected LAN-induced responses. Moreover, direct activation of dPHb-NAc projection during specific nighttime intervals over a three-week period independently from light exposure elicited depression-like manifestations, providing evidence for the pivotal role played by dpHb-NAc projection in LAN-induced negative mood. These findings further support Fernandez's conclusions regarding the great significance of the ipRGC-pHb circuit in mediating light-induced mood regulation [21].

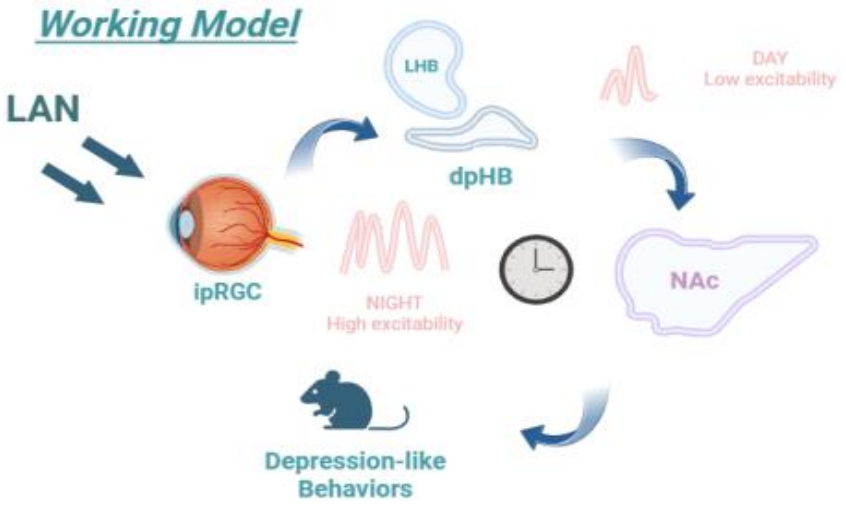

Figure 1. Working model of the ipRGC-dPHb-NAc circuit (Created with BioRender.com)

6. Conclusion

Light is crucial to most creatures on the Earth and has significant impact on circadian rhythm and mood modulation of humans. Sunlight resets the disturbed circadian system and relieve

uncomfortable reactions led by jet lag; Nocturnal light repress secretion of melatonin and therefore influence sleep quality negatively. In addition, light affects mood through the linking ipRGC to dorsal PHb. In research conducted by Fernandez D C et al., it is concluded that abnormal light exposure results in mood changes that are linked to modifications in PHb, and these alterations include heightened function of PHb neurons, prolonged the immediate-early gene c-Fos is upregulated in response to light stimulation, and disruption of the rhythmicity of clock genes. An K. et al. reveal the circuit ipRGC-dPHb-NAc (Figure 1) through series of experiments on mice, and conclude that the nocturnal light causes depressive-like behaviors in mice. It is speculated that prolonged exposure to artificial light during nighttime in humans may result in comparable alterations in neuronal activity, ultimately leading to impairments in mood regulation. This underscores the detrimental effects of irregular light stimulation on the natural circadian rhythm. These studies on light affecting mood might inspire scientists to invent new anti-depressants according to the ipRGC circuit instead of controlling neurotransmitters that most traditional medicines work to.

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