

Sleep Interrupted: How Our Modern Life Affects Our Rhythm

Melinda Fernyhough Culver*

OmniActive Health Technologies Inc., Morristown, New Jersey, USA

***Corresponding Author:** Melinda Fernyhough Culver, OmniActive Health Technologies Inc., Morristown, New Jersey, USA.

Received: March 05, 2018; **Published:** April 07, 2018

Abstract

Today, more people than ever before spend time under energy efficient lighting, working in front of computers, interacting with smartphones and watching television. Estimates from population studies indicate that the average American spends more than 10 hours per day viewing screens and the prevalence of digital device use is only increasing. Despite emitting substantially less blue light than natural sunlight, this dramatic rise in device usage begins to pose problems especially in terms of their effects on the circadian rhythm. This paper will explore some of the ways that light - especially blue light - affects sleep patterns.

Keywords: *High-Energy Blue Light; Circadian; Sleep; Diurnal; Artificial Light*

Abbreviations

MPOD: Macular Pigment Optical Density; UV: Ultraviolet; IR: Infrared; ipRGCs: Intrinsically Photosensitive Retinal Ganglion Cells

Introduction

Now, more than ever, we are awash in the light from a milieu of computers, smartphones, tablets, televisions, and energy efficient lighting. While this allows us to remain in contact with friends and family, have information readily at our fingertips, and maintain activity long after the sun has set on the day, these features of modern life are not without their disadvantages and problems. Estimates indicate that the average American spends more than 10 hours per day viewing screens and the prevalence of digital device use is only increasing [1]. In a recent survey, 90% of Americans reported using a technological device in the hour before bed with smartphones most popular among those under 30 leading to a skewing of this groups' sleep patterns [2]. The most common effect was delayed bedtime and shorter total sleep time and was consistently related to media use with interactive technologies (such as smartphones and tablets) more impactful compared to passive technologies (such as televisions) [2]. The ever-consuming need for media and its effects on sleep has affects all age groups. Many teenagers use multiple forms of technology late into the night and subsequently, their ability to stay alert and fully functional throughout the day is impaired - 33% of teenagers reported falling asleep during school in one study [3]. Screen time has been shown to be adversely associated with sleep outcomes in teens and children. Presence of a small screen, but not a TV, in the sleep environment and screen time were associated with perceived insufficient rest or sleep in school aged children cautioning against unlimited screen access in bedrooms [4]. Smartphone overuse has also been associated with depression and anxiety, and sleep quality may be affected [5].

Visible Light - Invisible Damage

Visible white light is composed of wavelengths of energy ranging from about 390 to 700 nanometers - each wavelength is perceived, by humans, to be a different color. On either end of the (human) visible spectrum lies ultraviolet (UV) and infrared (IR) wavelengths and, despite being invisible to us, other species readily see light in these ranges [6]. Indeed, one study looked at the lenses of 38 different mammals and found that some degree of UV sensitivity was present [7]. It has been proposed that humans have the ability to see UV light but it is blocked by absorbing pigments in the lens [8]. The compromise for lack of UV vision is protection from UV radiation for the sensitive color sensing parts of the eye.

The visible spectrum has its benefits beyond making the world colorful. Not only have claims been made about the perceptions, behaviors, and emotions that certain colors evoke [9] but color can also effect a physical change [10,11]. One wavelength range that has a strong influence on the body is the violet/blue range (390 - 500 nm) also known as high-energy blue light. Wavelengths at the lower end of this range can participate in the genesis of age-related macular degeneration, whereas wavelengths at the upper end beneficially influence alertness and the sleep/wake cycle. Indeed, the significant alerting effects of short-wavelength light in comparison to lights of longer wavelengths have been demonstrated [12]. Melatonin, one of the signals of the circadian cycle, is strongly influenced by light at the 460-484 nm range [13]. The largest source of high-energy blue light is sunlight; however, modern technology has brought a plethora of other sources of this damaging light.

Over the past two decades man-made sources have further increased the amounts of blue light to which we are exposed. For example, “cool” LED lights emit a large amount of light in the 420 - 500 nm range and compact fluorescent bulbs emit blue light in the 400-500 nm range. In addition to modern light sources, the ever-present digital device (400 - 520 nm), computer screen (420 - 520 nm), and television (400 - 520 nm) emit high-energy blue light (Figure 1) making it so that we are never more than a few inches away from danger [14].

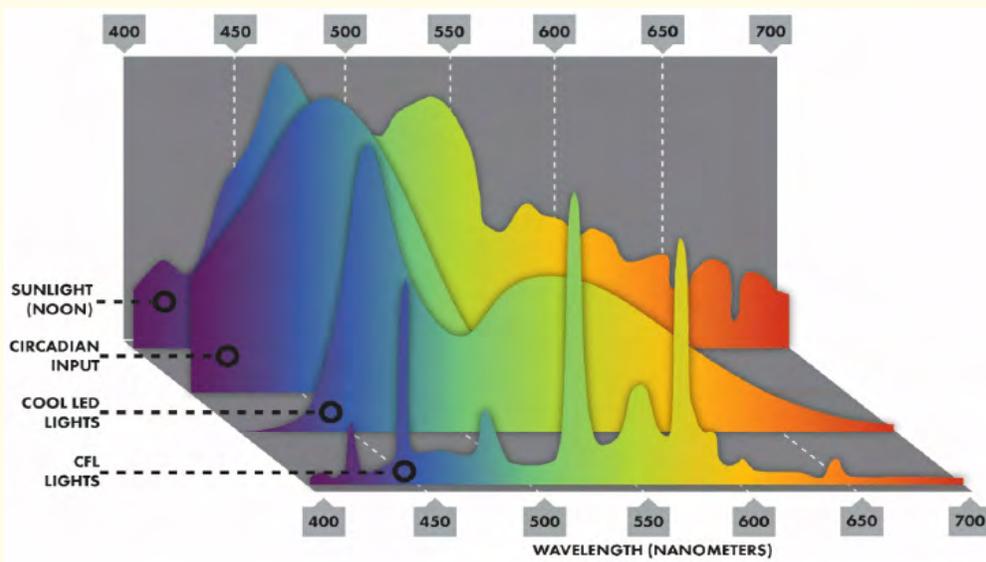


Figure 1: Common sources of high energy blue light. The largest source is the sun which has a peak of blue-light that provides a strong signal for circadian input. However, there are strong signals from LED lights as well as CFL lights that also strongly influences the circadian cycle.

The Eyes Have it: The Circadian Cycle

It has been said that the eyes are the window to the soul. True or not, the eyes certainly are the window to the brain - not only conveying visual information but also non-visual environmental clues that are important to keeping the internal clock on time. The internal clock - the circadian rhythm - is conserved in numerous species and drives a host of physiological and neuroendocrine responses. In humans, this cycle is close to, but not exactly, 24 h long. Indeed, the circadian (literally meaning about a day), has been demonstrated to be on average 24.2 h (23.5h - 24.7h) [15] meaning, eventually, one’s internal clock can become desynchronized from the diurnal rhythm. This endogenous rhythm requires exogenous input for adjustment in the form of light.

Circadian rhythm entrainment—the synchronizing of the biological clock with environmental cues—acts as a mechanism to reflect the natural periods of light and dark and impacts overall timing and duration of sleep and wakefulness [16]. The 24-hour pattern is predicated primarily on light and dark cycles that, for most of evolutionary history, have come from the sun and it was not until recently that exactly how this occurred was elucidated.

The retina has photoreceptors that allow for vision in low light (rods) as well as perceive color (cones). Recently, a third photoreceptor has been identified that plays no part in visual perception but rather helps regulate circadian rhythm [17]. These cells are called intrinsically photosensitive retinal ganglion cells (ipRGCs) and make up approximately 1-2% of the photoreceptor cells in the retina but are crucial for circadian rhythm entrainment [18]. These special photoreceptors are most sensitive to shorter wavelengths of light (470 - 480 nm) and express a photopigment called melanopsin [19] which performs a variety of non-image forming visual functions such as circadian control [20], mood and learning [21], the regulation of metabolism [22], and sleep modulation [23]. Once activated, ipRGCs signal the suprachiasmatic nuclei (SCN) - the region of the brain that acts as a circadian pacemaker - which, in turn, have numerous downstream targets [24]. One of these targets is the pineal gland such that stimulation by the SCN will inhibit release of melatonin.

Disrupting the Cycle

While light of any kind can suppress melatonin secretion, maximal suppression is at 460 nm with light in the 446 - 480 nm range strongly influencing melatonin release [25]. Indeed, night time exposure of 6.5 h of a monochromatic blue light (460 nm) suppressed melatonin twice as long as the same exposure to a monochromatic green light (555 nm) and shifted circadian rhythms by 3 h (vs. 1.5) [26]. Whereas the largest contributor to our daily exposure to high energy blue light is the sun, various common digital devices and energy-efficient lighting are also offenders of output in this range. For example, cool LED lights emit a large amount of light in the 420 - 500 nm range [25] and compact fluorescent bulbs emit blue light in the 400 - 500 nm range. In addition to modern light sources, common digital devices (400 - 520 nm), computer screens (420 - 520 nm), and televisions (400 - 520 nm) also emit high energy blue light (Figure 2).

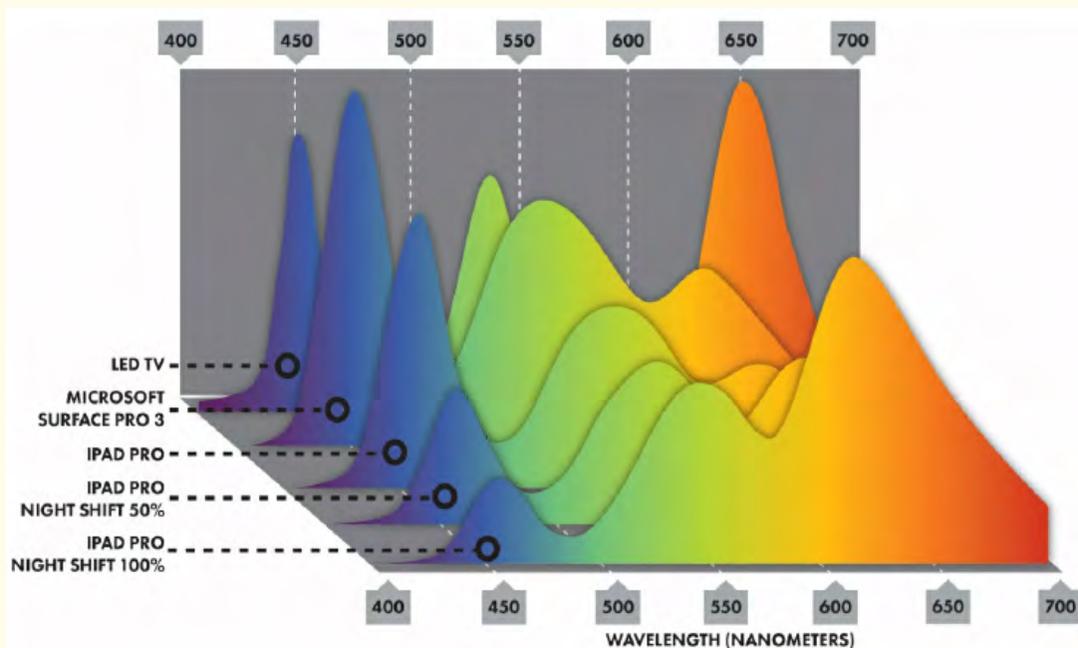


Figure 2: The light profile of common digital devices. Peaks of intensity around 460 nanometers correspond to the range of wavelengths known to provide circadian signaling. The use of features installed on many digital devices to reduce the amount of blue light emitted is also featured. As can be seen, this feature shifts the amount of blue light (or “white” light as we perceive it) towards the more golden hues. Despite this, there is some concern that the wavelengths in the 500-550 nanometer range are able to adversely influence the sleep wake cycle.

It has been reported that an iPad use suppresses melatonin by up to 7% in 1h and 23% in 2h [27]. With the addition of blue LED lights, melatonin suppression increases to 66% after 2h [27]. In a second study, 2h of evening computer use was disruptive to sleep continuity and increased daytime sleepiness in a group of participants [28]. In another study on the effects of a smartphone LED before bed, researchers found that melatonin release was delayed [29]. It is important to note, that not only is the wavelength of light emitted important but also the luminosity or lux. In one study, a 67% reduction of melatonin was noted with 1h of 1,000 lux at midnight (typical overcast day) and a 16% reduction with 200 lux (a well-lit living room) [30]. Furthermore, exposure to room light (< 200 lux) before bedtime not only delayed melatonin release by 90 min but also shortened melatonin duration in almost all of the study participants [31] underscoring how sensitive the circadian rhythm is to light. Though melatonin suppression is advantageous in the day as it enhances alertness, mis-timed high energy blue light can disrupt healthy circadian rhythms.

Sleep from Within - Melatonin

Deep within the geometric center the brain is the pineal gland and from this tiny gland, melatonin is produced and secreted. Melatonin is widely researched for a variety of actions and physiological effects [32]. In the absence of extraneous light cues, melatonin production in humans begins soon after sundown, peaks between 2 - 4 a.m. and ceases around 9 a.m. [33]. Indeed, almost 80% of the melatonin is produced at night whereas daytime production is low. Once synthesized, melatonin is quickly released into the systemic circulation as well as the cerebral spinal fluid where it modulates processes such as mood [34], sleep [35], body temperature [36], and food intake patterns [37]. Melatonin is a potent endogenous antioxidant that has shown to have more scavenging activity than vitamin E [38]. Additionally, melatonin has numerous positive peripheral effects including as an immunomodulatory [39] and anti-inflammatory [40].

Not only does melatonin secretion vary significantly during the lifetime of an individual but so too does the release of melatonin from external cues. Young children (1 - 3 yr) have been shown to have the highest nighttime melatonin with a sharp decrease in levels during the teenage years (15 - 20 yr) [41]. This also coincides with a shift toward an evening circadian preference and the onset of mood problems often occur during adolescence [42]. This shift of the circadian cycle begins earlier in females (as they enter puberty earlier) [43] and can reach a 1- to 4-hour delay in circadian rhythms during puberty [44]. In fact, subjects who were in late adolescence were less sensitive to dim light cues in the morning than their early adolescent counterparts [44] and are slower to fall asleep at night [45].

Sleep problems among older adults is well established and increased prevalence of sleep complaints has been observed in elderly subjects [46]. Even in the absence of clinically significant sleep disorders, healthy aging is associated with a decline in night-time sleep quality and duration, decreases in sleep depth, sleep intensity, and sleep continuity [47]. As we age, levels of reduced melatonin have been linked to age-related disturbances in the sleep-wake and temperature rhythms [41]. Indeed, the ability to synthesize melatonin is diminished during aging [48] such that low melatonin levels are considered a biomarker of aging [49]. In one study comparing postmenopausal women with and without insomnia, older subjects with insomnia had a 50 minute delay in the onset of melatonin secretion under dim light conditions - not only were the levels of melatonin lower in these subjects but the overall evening increases smaller [50]. It is suggested that age-related changes in sleep may be due to a weaker circadian regulation of sleep and wakefulness from a decline in visual sensitivity. Photopic sensitivity is known to decrease with age and it has been noted that in older individuals, sensitivity to wavelengths at 440 nm is diminished [51].

Supplementation of melatonin has been suggested for numerous modern-day issues including jet lag, insomnia, seasonal affective disorder, and shift-work. Ingestion of melatonin induces fatigue, sleepiness and a diminution of sleep latency within an hour after administration [35]. However, some studies have found limited benefit in melatonin supplementation [52]. Additionally, melatonin supplements on the market have been shown to be highly variable in melatonin content compared to what is claimed on the label [53]. The same study found that many products contained serotonin as an adulterant [53]. Drugs that alter serotonin levels are used in treating many mental health disorders and high levels of serotonin can be toxic. The presence of serotonin in melatonin supplement may confound current treatments or lead to toxicity.

It is known that numerous common foods contain melatonin [54] including herbs, vegetables, fruits such as cherries, apples and grapes, cereals such as rice, meat (lamb, beef, pork, chicken and fish), eggs, milk, wine and beer, and coffee and that consuming these foods will increase the circulating melatonin levels [55]. In fact, consuming foods high in melatonin can increase levels enough to have a positive effect on sleep [56] but it is unknown if this has an effect on the circadian rhythm.

Altered Reality - Changing the Environment

Changing the ambient lighting has been studied for effects on activity levels, sleep quality, and concentration. A study in a group of elderly residents, found that blue enriched lighting had both positive and negative effects. Ambient light enriched with blue light increased activity and reduced anxiety during the day but also increased nighttime activity and decreased sleep quality [57]. The color of light seems to affect the young and old differently. In older individuals, only blue light attenuated the release of nighttime melatonin whereas in young individuals both white and blue light resulted in decreased nighttime melatonin [58]. In one study, the effects of melatonin suppression in school age children was twice that of adults under similar conditions [59]. This would seem to suggest that lighting should be carefully considered when selecting lighting for different age groups.

In areas in which persons are expected to perform specific tasks (e.g. shift workers) or to maintain a level of mental alertness (students), the choice of ambient lighting may also have a large effect on for a positive outcome. While most studies looking at the results of light and blue light on melatonin levels found that blue light suppressed melatonin and subsequent sleepiness, the results on task-oriented behaviors, alertness, and cognition varied. In one study, sleepiness and melatonin declined in participants exposed to blue enriched white light compared to normal light which had a significant effect on memory errors, omission errors, and reaction times [60]. Yet another study that looked at the effects of blue light on reaction time and handgrip strength in athletes showed that although melatonin levels might be reduced in response to blue light, there was no effect on either parameter [61]. Exposure to blue enriched light induced greater melatonin suppression and enhanced subjective alertness and well-being in subjects resulting in significantly faster reaction times in tasks associated with sustained attention but not in tasks associated with executive function [62]. Despite the physiological arousal induced by light, it does not necessarily follow that cognitive improvement occurs and even might deteriorate accuracy in complex tasks [63].

An extremely common behavior in our electronic world is the evening use of digital devices. Modern computer screens, smartphones, tablets, and e-readers all emit large amounts of high energy blue light and are often used in a darkened room and a short distance from our eyes. In the evening, these devices may have the opposite effect than intended - keeping us awake rather than making us sleepy before bed. Indeed, a study on the effects of backlit LED computer screens demonstrated that sustained attention, working memory and attention, were significantly enhanced in the LED-backlit screen compared with the non-LED condition [64]. This same study also found that the LED computer screens suppressed the evening rise in melatonin and sleepiness. In a particularly telling study, the use of an e-reader before bedtime reduced evening sleepiness and melatonin secretion, thus taking longer to fall asleep and reducing alertness the following morning compared with reading a traditional paper book [65].

To offset this, many manufacturers have built in to the devices the ability to change the amount of blue light emitted from these devices. The use of this feature, and similar programs for computers, effectively reduces the amount of blue light and shifts the light towards the red end of the visible light spectrum (Figure 2). Although colors are perceived to be less vivid or are “golden” when this feature is activated it may help to reduce the depressive effects of these devices on melatonin and subsequent sleep pattern disruptions. Other methods to block a portion of the blue light emitting from these devices include filters that are placed directly onto the screen and the use of glasses fitted with amber lenses. The latter has shown some efficacy. Over 7 d, users who wore amber lens glasses had better overall sleep quality, soundness of sleep, and total sleep time compared with those who wore clear lenses [66]. These results echo a similar study in which lenses designed to block blue light significantly attenuated LED-induced melatonin suppression in the evening and decreased vigilant attention and subjective alertness before bedtime compared to clear lenses [23].

In a seemingly portended manner, nature has provided a mechanism by which the effects of high energy blue light may be attenuated - carotenoids. Carotenoids are organic pigments that are mostly produced by plants and algae and are divided into two general classes - carotenes and xanthophylls. Due to their red-yellow color, carotenoids generally absorb wavelength in the ~400 - 550 nm range (violet to green light) and serve two roles in plants and algae - absorption of light energy and protection of chlorophyll from photodamage. Of the more than 700 carotenoids found in nature there are ~ 30 that are found in the diet. Carotenoids that are absorbed from the diet can be stored in fatty tissue serving as an additional source if consumed.

Of all the carotenoids, only three are found in the eye - lutein, RR-zeaxanthin, and RS (meso)-zeaxanthin. These three carotenoids are deposited in the macular region of the retina and, as they do in plants, act as potent antioxidants and filters of high energy blue light. Specifically, lutein absorbs light in the 420 - 470 nm range whereas the zeaxanthin isomers absorb between 430 - 480 nm underscoring the need to provide all three macular carotenoids to absorb a broad range of blue light. The blue-light filtering action of these carotenoids may contribute to the complex interaction of light and circadian rhythm. In fact, in one study, it was demonstrated that supplementation with lutein, zeaxanthin, and mesozeaxanthin for 3 months improved overall sleep quality in those with high digital device use [67] as well as increased melatonin after 6 months (unpublished observations). As these carotenoids are exclusively found in the diet, this may be one mechanism by which sleep can be supported naturally.

Conclusion

Blue light has widespread rippling effects that span many aspects of our lives. The modern environment and digital devices that are ubiquitous and pervasive are wreaking havoc on our ability to fall asleep - and stay asleep - having repercussions for the subsequent day's productivity. The mechanism by which this occurs is based on the ancient system of the largest source of blue light - the sun - and the signals the brain receives to stay alert or to begin sleeping. Although there are several ways by which we can ameliorate some of these effects, we must still be mindful of the consequences digital devices have on us.

Conflict of Interest

The author states there are no conflict of interests.

Bibliography

1. The Nielsen Total Audience Report Q1. The Nielsen Total Audience Report (2016).
2. Gradisar M., *et al.* "The sleep and technology use of Americans: findings from the National Sleep Foundation's 2011 Sleep in America poll". *Journal of Clinical Sleep Medicine* 9.12 (2013): 1291-1299.
3. Calamaro CJ., *et al.* "Adolescents living the 24/7 lifestyle: effects of caffeine and technology on sleep duration and daytime functioning". *Pediatrics* 123.6 (2009): e1005-e1010.
4. Falbe J., *et al.* "Sleep duration, restfulness, and screens in the sleep environment". *Pediatrics* 135.2 (2015): e367-e375.
5. Demirci K., *et al.* "Relationship of smartphone use severity with sleep quality, depression, and anxiety in university students". *Journal of Behavioral Addictions* 4.2 (2015): 85-92.
6. Pye D. "To add another hue unto the rainbow-near ultraviolet in nature". *Optics and Laser Technology* 43.2 (2011): 310-316.
7. Douglas RH and G Jeffery. "The spectral transmission of ocular media suggests ultraviolet sensitivity is widespread among mammals". *Proceedings of the Royal Society B: Biological Sciences* 281.1780 (2014).
8. Griswold MS and WS Stark. "Scotopic spectral sensitivity of phakic and aphakic observers extending into the near ultraviolet". *Vision Research* 32.9 (1992): 1739-1743.

9. Han S and D Lee. "The effects of treatment room lighting color on time perception and emotion". *Journal of Physical Therapy Science* 29.7 (2017): 1247-1249.
10. Rohringer S., et al. "The impact of wavelengths of LED light-therapy on endothelial cells". *Scientific Reports* 7.1 (2017): 10700.
11. Kim SK., et al. "Skin photorejuvenation effects of light-emitting diodes (LEDs): a comparative study of yellow and red LEDs in vitro and in vivo". *Clinical and Experimental Dermatology* 41.7 (2016): 798-805.
12. Šmotek M., et al. "Does blue-light increase cortical activation? Findings from an EEG study". *Sleep Medicine* 40 (2017): e310-e311.
13. Lockley SW., et al. "Short-wavelength sensitivity for the direct effects of light on alertness, vigilance, and the waking electroencephalogram in humans". *Sleep* 29.2 (2006): 161-168.
14. Loughheed T. "Hidden blue hazard? LED lighting and retinal damage in rats". *Environmental Health Perspectives* 122.3 (2014): A81.
15. Czeisler CA., et al. "Stability, precision, and near-24-hour period of the human circadian pacemaker". *Science* 284.5423 (1999): 2177-2181.
16. Golombek DA and RE Rosenstein. "Physiology of circadian entrainment". *Physiological Reviews* 90.3 (2010): 1063-1102.
17. Altimus CM., et al. "Rods-cones and melanopsin detect light and dark to modulate sleep independent of image formation". *Proceedings of the National Academy of Sciences of the United States of America* 105.50 (2008): 19998-20003.
18. Tosini G., et al. "Effects of blue light on the circadian system and eye physiology". *Molecular Vision* 22 (2016): 61-72.
19. Enezi J., et al. "A "melanopic" spectral efficiency function predicts the sensitivity of melanopsin photoreceptors to polychromatic lights". *Journal of Biological Rhythms* 26.4 (2011): 314-323.
20. Dijk DJ and SN Archer. "Light, sleep, and circadian rhythms: together again". *PLoS Biology* 7.6 (2009): e1000145.
21. Meng Q., et al. "Blue light filtered white light induces depression-like responses and temporary spatial learning deficits in rats". *Photochemical and Photobiological Sciences* (2018).
22. Ayturk DG., et al. "Lack of Melanopsin Is Associated with Extreme Weight Loss in Mice upon Dietary Challenge". *PLoS One* 10.5 (2015): e0127031.
23. Ostrin LA., et al. "Attenuation of short wavelengths alters sleep and the ipRGC pupil response". *Ophthalmic and Physiological Optics* 37.4 (2017): 440-450.
24. LeGates TA., et al. "Light as a central modulator of circadian rhythms, sleep and affect". *Nature Reviews Neuroscience* 15 (2014): 443-454.
25. West KE., et al. "Blue light from light-emitting diodes elicits a dose-dependent suppression of melatonin in humans". *Journal of Applied Physiology* 110.3 (2011): 619-626.
26. Lockley SW., et al. "High sensitivity of the human circadian melatonin rhythm to resetting by short wavelength light". *Journal of Clinical Endocrinology and Metabolism* 88.9 (2003): 4502-4505.
27. Wood B., et al. "Light level and duration of exposure determine the impact of self-luminous tablets on melatonin suppression". *Applied Ergonomics* 44.2 (2013): 237-240.
28. Green A., et al. "Evening light exposure to computer screens disrupts human sleep, biological rhythms, and attention abilities". *Chronobiology International* 34.7 (2017): 855-865.

29. Heo JY, *et al.* "Effects of smartphone use with and without blue light at night in healthy adults: A randomized, double-blind, cross-over, placebo-controlled comparison". *Journal of Psychiatric Research* 87 (2017): 61-70.
30. McIntyre IM, *et al.* "Human Melatonin Suppression by Light is Intensity Dependent". *Journal of Pineal Research* 6.2 (1989): 149-156.
31. Gooley JJ, *et al.* "Exposure to Room Light before Bedtime Suppresses Melatonin Onset and Shortens Melatonin Duration in Humans". *The Journal of Clinical Endocrinology and Metabolism* 96.3 (2011): E463-E472.
32. Posadzki PP, *et al.* "Melatonin and health: an umbrella review of health outcomes and biological mechanisms of action". *BMC Medicine* 16.1 (2018): 18.
33. Brzezinski A. "Melatonin in humans". *New England Journal of Medicine* 336.3 (1997): 186-195.
34. Tapia-Osorio A, *et al.* "Disruption of circadian rhythms due to chronic constant light leads to depressive and anxiety-like behaviors in the rat". *Behavioural Brain Research* 252 (2013): 1-9.
35. Zhdanova IV, *et al.* "Melatonin: a sleep-promoting hormone". *Sleep* 20.10 (1997): 899-907.
36. Cuesta M, *et al.* "Skin Temperature Rhythms in Humans Respond to Changes in the Timing of Sleep and Light". *Journal of Biological Rhythms* 32.3 (2017): 257-273.
37. Baron KG, *et al.* "Circadian timing and alignment in healthy adults: associations with BMI, body fat, caloric intake and physical activity". *International Journal of Obesity* 41.2 (2017): 203-209.
38. Pieri C, *et al.* "Melatonin: a peroxy radical scavenger more effective than vitamin E". *Life Science* 55.15 (1994): PL271-PL276.
39. Tordjman S, *et al.* "Melatonin: Pharmacology, Functions and Therapeutic Benefits". *Current Neuropharmacology* 15.3 (2017): 434-443.
40. Favero G, *et al.* "Melatonin as an Anti-Inflammatory Agent Modulating Inflammasome Activation". *International Journal of Endocrinology* (2017): 1835195.
41. Waldhauser F, *et al.* "Alterations in Nocturnal Serum Melatonin Levels In Humans With Growth and Aging". *The Journal of Clinical Endocrinology and Metabolism* 66.3 (1988): 648-652.
42. Dolsen MR and AG Harvey. "Dim Light Melatonin Onset and Affect in Adolescents With an Evening Circadian Preference". *Journal of Adolescent Health* 62.1 (2018): 94-99.
43. Roenneberg T, *et al.* "A marker for the end of adolescence". *Current Biology* 14.24 (2004): R1038-R1039.
44. Hagenauer MH, *et al.* "Adolescent Changes in the Homeostatic and Circadian Regulation of Sleep". *Developmental Neuroscience* 31.4 (2009): 276-284.
45. Taylor DJ, *et al.* "Sleep tendency during extended wakefulness: insights into adolescent sleep regulation and behavior". *Journal of Sleep Research* 14.3 (2005): 239-244.
46. Roepke SK and S Ancoli-Israel. "Sleep disorders in the elderly". *Indian Journal of Medical Research* 131 (2010): 302-310.
47. Bliwise DL, *et al.* "Age changes in timing and 24-hour distribution of self-reported sleep". *American Journal of Geriatrics Psychiatry* 13.12 (2005): 1077-1082.

48. Paltsev MA., *et al.* "Morphofunctional and signaling molecules overlap of the pineal gland and thymus: role and significance in aging". *Oncotarget* 7.11 (2016): 11972-11983.
49. Sharma M., *et al.* Circadian rhythms of melatonin and cortisol in aging". *Biological Psychiatry* 25.3 (1989): 305-319.
50. Jehan S., *et al.* "Sleep, Melatonin, and the Menopausal Transition: What Are the Links?" *Sleep Science* 10.1 (2017): 11-18.
51. Hammond BR., *et al.* "Preservation of visual sensitivity of older subjects: association with macular pigment density". *Investigative Ophthalmology and Visual Science* 39.2 (1998): 397-406.
52. Liira J., *et al.* "Pharmacological interventions for sleepiness and sleep disturbances caused by shift work". *Cochrane Database of Systematic Reviews* 8 (2014): Cd009776.
53. Erland LA and PK Saxena. "Melatonin Natural Health Products and Supplements: Presence of Serotonin and Significant Variability of Melatonin Content". *Journal of Clinical Sleep Medicine* 13.2 (2017): 275-281.
54. Meng X., *et al.* "Dietary Sources and Bioactivities of Melatonin". *Nutrients* 9.4 (2017): E367.
55. Oba S., *et al.* "Consumption of vegetables alters morning urinary 6-sulfatoxymelatonin concentration". *Journal of Pineal Research* 45.1 (2008): 17-23.
56. Howatson G., *et al.* "Effect of tart cherry juice (*Prunus cerasus*) on melatonin levels and enhanced sleep quality". *European Journal of Nutrition* 51.8 (2012): 909-916.
57. Hopkins S., *et al.* "Blue-Enriched Lighting for Older People Living in Care Homes: Effect on Activity, Actigraphic Sleep, Mood and Alertness". *Current Alzheimer Research* 14.10 (2017): 1053-1062.
58. Gabel V., *et al.* "Differential impact in young and older individuals of blue-enriched white light on circadian physiology and alertness during sustained wakefulness". *Scientific Reports* 7.1 (2017): 7620.
59. Higuchi S., *et al.* "Influence of light at night on melatonin suppression in children". *Journal of Clinical Endocrinology and Metabolism* 99.9 (2014): 3298-3303.
60. Motamedzadeh M., *et al.* "The effect of blue-enriched white light on cognitive performances and sleepiness of night-shift workers: A field study". *Physiology and Behavior* 177 (2017): 208-214.
61. Knaier R., *et al.* "Effects of bright and blue light on acoustic reaction time and maximum handgrip strength in male athletes: a randomized controlled trial". *European Journal of Applied Physiology* 117.8 (2017): 1689-1696.
62. Chellappa SL., *et al.* "Non-visual effects of light on melatonin, alertness and cognitive performance: can blue-enriched light keep us alert?" *PLoS One* 6.1 (2011): e16429.
63. Rodriguez-Morilla B., *et al.* "Blue-Enriched White Light Enhances Physiological Arousal But Not Behavioral Performance during Simulated Driving at Early Night". *Frontiers in Psychology* 8 (2017): 997.
64. Cajochen C., *et al.* "Evening exposure to a light-emitting diodes (LED)-backlit computer screen affects circadian physiology and cognitive performance". *Journal of Applied Physiology* (1985) 110.5 (2011): 1432-1438.
65. Chang AM., *et al.* "Evening use of light-emitting eReaders negatively affects sleep, circadian timing, and next-morning alertness". *Proceedings of the National Academy of Sciences of the United States of America* 112.4 (2015): 1232-1237.
66. Shechter A., *et al.* "Blocking nocturnal blue light for insomnia: A randomized controlled trial". *Journal of Psychiatric Research* 96 (2018): 196-202.

67. Stringham JM., *et al.* "Macular Carotenoid Supplementation Improves Visual Performance, Sleep Quality, and Adverse Physical Symptoms in Those with High Screen Time Exposure". *Foods* 6.7 (2017): E47.

Volume 13 Issue 5 May 2018

©All rights reserved by Melinda Fernyhough Culver.