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WHAT IS "HEALTHY LIGHTING?"

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It is well-known that the light/dark cycle incident on the retina regulates the timing of the human circadian system. Disruption of a regular, 24-hour pattern of light and dark can significantly affect our health and well-being. A wide range of modern maladies, from sleep disorders to cancer, have been linked to light-induced circadian disruption. Light has been defined, however, only in terms of the human visual system, not the circadian system. Thus, the study of light-induced circadian disruption is in need of a new definition of light (and dark). Here we contrast light as a stimulus for the human visual system with that for the human circadian system to elucidate the significance of developing a new definition of circadian light as it might ultimately be used to improve health and well-being.

Keywords: circadian system; visual system; melatonin; delayed sleep phase disorder; seasonal affective disorder; advanced sleep phase disorder

Introduction

Because the Earth rotates on its axis, there is a regular and predictable 24-hour pattern of daylight and darkness over most of its surface. Terrestrial species have adapted to this daily pattern by evolving biological rhythms that repeat at approximately 24-hour intervals.[1] These rhythms are called circadian rhythms, from the Latin *circa* (about) and *dies* (day), and reflect a very tight coupling between the natural environmental light-dark pattern and the cyclicity of the endogenous master clock, the suprachiasmatic nuclei (SCN), a small portion of the hypothalamus of the brain. The master clock governs a wide range of biological cycles, from cell division, to hormone production, to behavior (e.g., sleep-wake) that, when synchronized with the natural light/dark cycle, enables the organism to entrain these cycles to its particular photic niche (diurnal or nocturnal) and to its location on Earth. Although the period of the solar cycle is almost exactly 24-hours, the period of the internal, genetically self-governing master clock is slightly longer than 24 hours in most diurnal species and slightly shorter in most nocturnal species.

A wide variety of anatomical and physiological, as well as behavioral (night-active vs. day-active), characteristics are, not coincidentally, associated with the intrinsic period of the master clock[2], including the retinal mechanisms that support both the visual and circadian systems of nocturnal and diurnal species. For example, the circadian phototransduction mechanisms for nocturnal species are nearly 3000 times more sensitive to light than those of diurnal species.[3] Thus, very low levels of light can entrain the circadian system of a mouse whereas much higher levels are needed for humans.[4] In this way, humans can avoid false-positive light input to the circadian system during the night (e.g., fire light) and mice can avoid false-negative light input at early dawn and late twilight. Furthermore, since the retinal photopigments underlying circadian phototransduction differ between species, light as it affects the circadian system of a nocturnal animal, like a mouse, is quite different than light as it affects the circadian system of humans. [4,5] Mice, for example, have photopigment maximally sensitive to ultraviolet radiation, prevalent in the sky during dawn and dusk, whereas humans are insensitive to ultraviolet radiation. Within species too, the neural machinery of the retina needed to process light for the visual system and needed for the circadian system are quite distinct, even though the two systems share at least some of the same retinal photopigments. [4,5] In humans for example, the circadian system receives input from the short-wavelength (S) cone and, consequently, is maximally sensitive to radiation close to this photoreceptor's peak spectral sensitivity, which is about 450 nm. Although the human visual system receives input from all three cone types, the visual channel used to read, for example, receives minimal input from the S cone and is maximally sensitive to middle-wavelength (555 nm) light, representing the combined input of the long-wavelength (L) and medium-wavelength (M) cones. Since the phototransduction mechanisms differ both *among* species and *within* species, the very definition of light as a photic stimulus also differs both *among* and *within* species.

One goal of this chapter is to elucidate more clearly the differences between light as a stimulus for the human visual system and light as a stimulus for the human circadian system. Circadian light cannot be defined in terms of current photometric quantities (lux, lumens, luminance) because the phototransduction mechanisms associated with vision, which underlie conventional photometry, are different than those associated with the circadian system. A second goal is to provide a deeper appreciation for the significance of the biological consequences of disrupting circadian rhythms as they might be affected by the electric and natural light sources that illuminate daytime and nighttime built environments. The need for this understanding is becoming increasingly clear as more clinical data demonstrate that disruption of a regular, 24-hour pattern of light and dark leads to wide variety of health- and performance-related problems in humans. To begin this discussion, it is important to first have a brief overview of the phototransduction mechanisms to and the output rhythms from the circadian system.

Input Pathways to the Circadian System

Photoreceptors in the mammalian retina convert light into neural signals sent via the retinohypothalamic tract (RHT) to the master clock in the SCN. The well-known visual photoreceptors, rods (operating at low, scotopic light level) and cones (operating at high, photopic light level), and a recently discovered intrinsically photosensitive retinal ganglion cell (ipRGC)[6] all participate in the conversion of retinal light exposures into neural signals for the SCN, a phenomenon called circadian phototransduction.[7]

The ipRGC neurons directly convert light into neural signals in mammals and, as shown experimentally, can still provide light/dark entraining information to the SCN in the absence of functional rods and cones.[8] Normally, the ipRGCs in humans receive input from the cones through a spectrally-opponent mechanism that underlies human color vision.[4,9,10] The threshold for participation in circadian phototransduction by this spectrally opponent mechanism appears to be controlled by a neural mechanism in the retina similar to that which determines whether rods or cones will provide scotopic or photopic input to the visual system.

There are two spectrally-opponent cone mechanisms underlying trichromatic human color vision: a blue vs yellow channel and a red vs green channel. Signals from the three cone photoreceptor types are combined by post-receptor retinal neurons to code color vision. Within the retina these signals combine in an antagonistic way to form the red vs green (L – M) and the blue vs yellow [S – (L+M)] spectrally-opponent channels. These spectrally-opponent channels combine with the achromatic channel (primarily L and M) to produce our perceptions of brightness. Because of the spectrally-opponent input, the apparent brightness of lights of different spectral power distributions exhibits what is called subadditivity, whereby under certain conditions adding more light can actually reduce the brightness response of the visual system. Subadditivity by the visual system is demonstrated by comparing the apparent brightness of polychromatic lights to the apparent brightness of each narrow-band spectral component. Under some conditions the combination of two narrow-band spectra together will appear less bright than either of the two narrow-band spectra alone.[10]

Subadditivity is also exhibited by the human circadian system because it receives input from at least one of these spectrally-opponent color channels. The blue vs yellow channel seems to provide input to the human ipRGC, giving the human circadian system a peak spectral sensitivity at about 450 nm and a subadditive response to white light.[11] Although much more needs to be discovered about the neural mechanisms underlying circadian phototransduction, input from the blue vs yellow channel appears to be controlled by a neural mechanism in the retina similar to that which transitions the visual system from the scotopic (rod) to the photopic (cone) operating ranges. A model of circadian phototransduction has been developed and used to predict the effectiveness of both narrow-band and polychromatic lights for stimulating the human circadian system

and independent data were subsequently gathered that are consistent with predictions from the model. [10,11]

Some Output Rhythms Affected by the Circadian System

Output rhythms are behavioral and physiological rhythms regulated by the SCN, such as sleep, alertness, core body temperature, locomotor activity, feeding and drinking, and hormone production. A regular 24-hour pattern of light and dark will entrain and orchestrate these rhythms under normal conditions.

Sleep/wake cycle

The sleep/wake cycle is one of the most obvious circadian rhythms and defines a species' photic niche; diurnal species are awake during the day and asleep at night whereas nocturnal species are asleep during the day and awake at night. Most species, including humans, are under the influence of two systems: the sleep drive (homeostatic) and the alerting force (circadian).[12] The sleep drive and the alerting force are distinct and independent from each other, although they normally work in concert to ensure that individuals fall asleep at night and are awake during the day. The sleep drive is normally low when people get up in the morning and increases steadily throughout the waking day. The alerting force is regulated by the SCN and, thus, follows a strong circadian rhythm, reaching a peak during the early evening and a trough during the second half of the night. Under normal conditions the close orchestration of the timing of the sleep drive and the timing of the alerting force determines when individuals fall asleep and how well they sleep at night. Because the sleep/wake cycle, and more general behavior, is under control of two distinct mechanisms, is it not an ideal marker for circadian system response. People can be awake and active when their alerting force is low and asleep when it is high. Other markers of circadian timing, like core body temperature and melatonin secretion, are often preferred to behavioral measures, like the sleep/wake cycle, because they are less susceptible to what is termed "masking," whereby extraneous factors compromise valid inferences about circadian timing.

Core body temperature

Core body temperature is governed by the hypothalamus and varies with a circadian pattern. Temperatures are high during the day, reach a peak in the early evening and then decline to a nadir about two hours before one naturally wakes up. Core body temperature is typically in synchrony with the alerting force from the SCN. Therefore, core body temperature is often used as a primary measure of circadian timing. Although core body temperature is less susceptible to masking, it is not impervious to other extraneous variables such as digestion and exercise. Core body temperature readings are also difficult to obtain because they are typically acquired through rectal probes. Controversy exists too as to whether core body temperatures gathered by this technique are really indicative of inter-cranial temperatures that are most closely regulated by the hypothalamus.

Hormone production

Although there is strong evidence that the master clock influences the circadian rhythms of a wide variety of hormones, most measures of circadian timing are based upon concentration measurements of the hormone melatonin synthesized by the pineal gland. The pineal gland is located near the center of the brain, is about the size of a pea and has a shape resembling that of a pine cone, thus its name. It is believed that the primary function of the pineal gland is to convey light/dark information to the body via night-time secretions of the hormone melatonin.[13] Melatonin is easily absorbed into the bloodstream, which makes it an ideal chemical messenger of time of day information to the entire body. Melatonin also participates in the transmission of information concerning day length or photoperiod for the organization of seasonal responses in some species (e.g., breeding).

Melatonin is only produced at night *and* under conditions of darkness.[12] Under normal conditions, changes in melatonin concentrations are approximately inversely related to changes in core body temperature in humans; peak levels typically occur at night slightly before core body temperature troughs. Melatonin concentrations, as well as those of other hormones such as cortisol, are measured in a wide variety of body fluids; blood plasma and saliva are the two most practical sources for melatonin concentration measurements. Unlike other hormones, however, melatonin appears to be almost exclusively regulated by the SCN. Since the response of the SCN is strongly affected by retinal light exposures, the (masking) effect of light on melatonin synthesis at night has been used as the primary measure of circadian system's response to light. It is now well established that modulation of light level and light spectrum will induce dose-response, graded changes in melatonin concentrations at night. For practical and for theoretical reasons then, most of the discussion in the literature about the impact of light on the circadian system is based upon suppression of melatonin production by the pineal gland at night.

Light as a Physical Quantity

Surprisingly perhaps, light is narrowly and formally defined in terms of human vision, and its definition is based upon psychophysical experiments investigating the spectral sensitivity of the eye that were conducted nearly a century ago.[14,15] Strictly speaking then, light has no meaning for plants and other animals. Nevertheless, light is commonly used to describe any and all optical radiation between approximately 380 nm and 730 nm even though, for example, some plants and animals have sensitivity to optical radiation outside this region. People often, erroneously, use adjectives to expand this spectral range with such terms as "ultraviolet light" or "infrared light," both of which are oxymorons. Since neither ultraviolet nor infrared radiation can be seen by humans, optical radiation in these bands cannot be light, by definition.

Even for humans, the formal definition for light is quite limiting. The human visual system is very complex and will exhibit a multitude of spectral sensitivity functions

depending upon a range of spectral-spatial-temporal factors associated with that optical radiation. For example, the apparent brightness of a small blue disc of light seen by the fovea will appear dimmer than that same disc seen in the periphery.[16] Over the last century a large number of human visual spectral sensitivity functions have been identified. To, at least in part, address this complexity, a handful of spectral sensitivity functions have been formally accepted as luminous efficiency functions for optical radiation and, perhaps surprisingly, as alternative definitions for light. [14,17,18] Figure 1 shows the currently accepted luminous efficiency functions that underlie alternative, formal definitions of light, which can, and have, led to significant confusion among non-specialists. Also shown in Figure 1 is the modeled spectral sensitivity of the human circadian system to polychromatic white light.

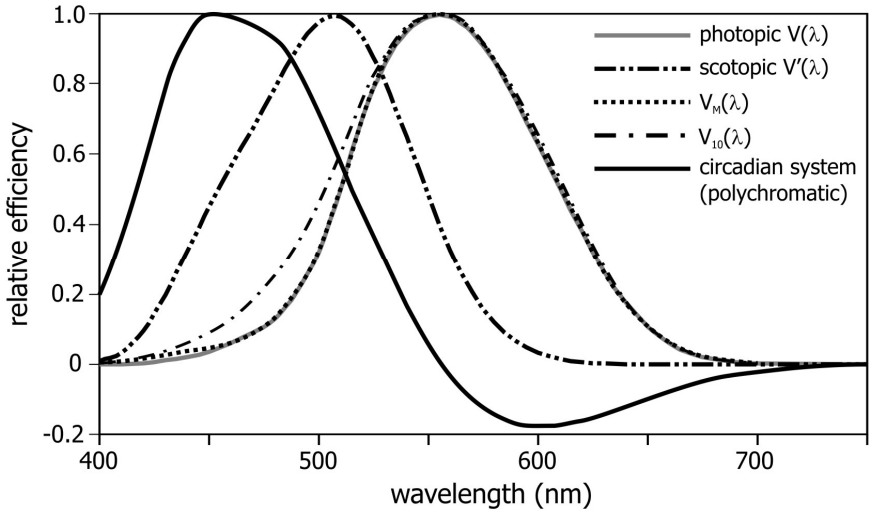

Figure 1: Four luminous efficiency functions sanctioned by the Commission Internationale de l'Eclairage (CIE)[13,16,17] together with the spectral sensitivity of the human circadian system to polychromatic, white light according to the model of circadian phototransduction by Rea et al., 2005.[11] The photopic luminous efficiency function (V(λ)) is the standard spectral weighting function for all commercially available light meters and also characterizes the spectral sensitivity of the human fovea for visual performance tasks (e.g., simple reaction times or reading alpha numeric text) where the speed and accuracy of processing information are measured.

V(λ) is the oldest of these luminous efficiency functions and underlies the definition of light used in commerce and by all government regulatory agencies. Thus, when a lamp manufacturer publishes the number of *lumens* generated by a source, V(λ) is used to spectrally weight its optical radiation. When government agencies regulate the *luminous efficacy* of a light source, the *illuminance* needed for an application (e.g., a roadway intersection) or the *luminous intensity* of a signal light, V(λ) is used to spectrally weight the optical radiation from practical light sources in all of these regulations. Significantly then, when one purchases a light source or is legally constrained in the application of that source, V(λ) is the embedded in every lighting specification.

Because the formal definition of light does not represent the spectral sensitivities of plants, animals and, indeed, the complexity of the human visual system, $V(\lambda)$ is an incomplete and potentially misleading characterization of optical radiation from sources used to grow plants and animals and even to provide visual sensations to humans. To add further weight to this problem, and as already discussed, light is necessary to control the daily cycles of all human biological functions.[9] Circadian rhythms are governed by retinal phototransduction mechanisms quite distinct from those underlying $V(\lambda)$. Because science and medicine have increasingly shown the importance of circadian rhythms for health and well-being in humans, it is likewise increasingly important for manufacturers and regulatory bodies to expand their definitions of light to include spectrally-weighted optical radiation that entrains the human circadian system.

In order to fully understand the importance that light has on the biological system, it is first necessary to consider optical radiation in terms of its fundamental physical properties. For the purposes of this chapter and for practical convenience, light can be decomposed into five basic characteristics[19,20]:

- Quantity
- Spectrum
- Spatial distribution
- Timing
- Duration

Light Characteristics as They Affect the Human Visual and Circadian Systems

As previously noted, the natural 24-hour light/dark cycle is the master clock's main synchronizer for its host's photic niche and location on earth. To more precisely understand how this synchronization occurs, it is necessary to understand the physical characteristics of light incident on the retina and, in these terms, how light is processed by the host's retina. Because light is formally defined in terms of the human visual system[17], and because the human species is of primary interest for lighting technology development, it is useful to contrast how each characteristic of light is processed by the human visual system and by the human circadian system.

Quantity

The human visual system can operate over the entire, very large range of levels of light available on the earth's surface, from starlight (0.00001 lx) to bright sunshine on a snow-covered mountain (100,000 lx), about 10 to 12 orders of magnitude. Typical levels provided by electric light sources, both indoors and out, are in the middle of this range, from about 0.1 lx to 1000 lx. Although the visual system operates better at higher levels, it does so with a diminishing return. Several studies (e.g.[21]) have shown, for example, that visual performance, the speed and accuracy of processing visual information, is near its maximum at typical office illuminance levels (500 lx on the task surface or

approximately 100 lx at the cornea) using commercially available "white" light sources. In contrast, these same levels and sources provide light only near the threshold of circadian system activation (***T*** in Figure 2), which is approximately 30 lx at the cornea with natural pupils (≈4 mm diameter) from a white light source.

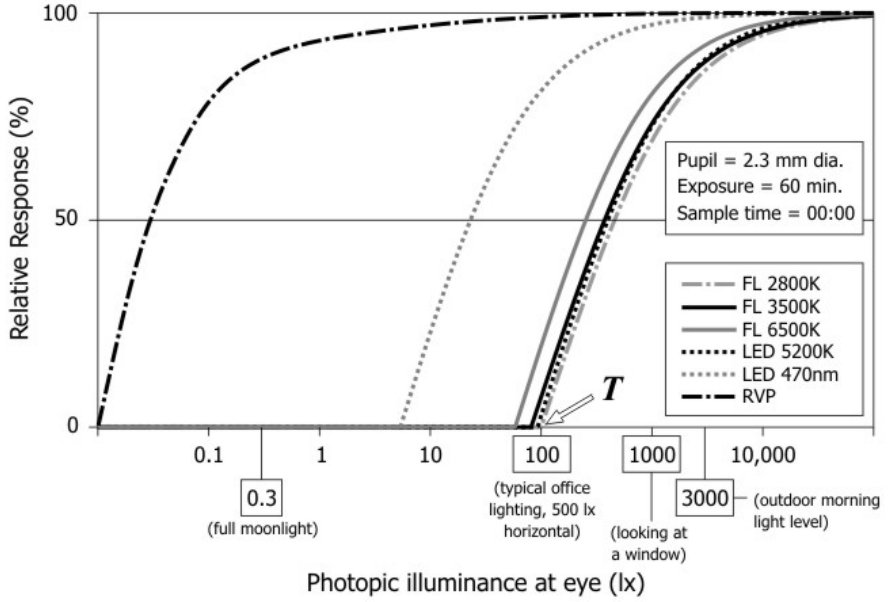

Figure 2: Relative response functions from the human visual and circadian systems plotted as function of photopic illuminance (in lx) measured at the cornea. The relative visual performance (RVP) function represents the speed and accuracy of processing visual information for a task (e.g., reading alphanumeric text) illuminated by *any* white light source. The remaining functions represent the relative suppression response by nocturnal melatonin to lights of different spectral composition; four white light sources, three fluorescent (FL) and one light emitting diode (LED), of different correlated color temperatures (CCT) in, kelvin (K), and one blue (λ_{max} = 470 nm) LED. The model assumes a fixed pupil size of 2.3 mm in diameter, 60 minute exposure at midnight, when melatonin levels are rising. Typical illuminance levels one might experience during the day supplement the abscissa. The symbol ***T*** indicates the approximate threshold light level from a "white" light source like those illustrated in the figure, with natural pupils of 4 mm in diameter, for circadian system activation.

Spectrum

Visual performance is most efficient for light in the middle of the visible spectrum with a spectral sensitivity closely matching the photopic luminous efficiency function peaking at 555 nm shown in Figure 1. The human circadian system, on the other hand, is most sensitive to much shorter wavelengths, near about 450 nm[11] and, as previously discussed, exhibits subadditivity. As illustrated in Figure 1, the circadian system spectral sensitivity has a negative lobe from about 550 nm to 700 nm.[4] When spectral energy in this long-wavelength range is combined with spectral energy at short wavelengths, the net impact of the short-wavelength energy on the circadian system response is reduced. In general

then, different practical light sources with the same efficiency for the visual performance can vary quite considerably in terms of their efficiency for stimulating the circadian system and vice versa.

As previously described, a general model of circadian light from any spectral power distribution and irradiance has been published[9,11] and it is possible to compare practical light sources in terms of the efficacy for stimulating the circadian system. Table 1 shows the relative amount of corneal (photopic) illuminance needed to produce a criterion response by the human circadian system (50% melatonin suppression for one hour exposure with a pupil diameter of 2.3 mm). In general, the more the source is dominated by short wavelengths the lower the illuminance required to reach a criterion response; compare for example two "white" fluorescent lamps of different correlated color temperatures (CCT), the 8000 K lamp and the 2700 K compact fluorescent lamp. For these two examples, it takes nearly three times the illuminance and three times the electric power to produce the same circadian response. Not unexpectedly then, the blue LED is the most efficacious light source for stimulating the human circadian system. One peculiarity should be noted in the table. There is an intransitivity between CCT and circadian effectiveness as shown by the higher required illuminance for the 4100 K lamp than for the 3350 K lamp. This intransitivity is associated with the subadditve response of the circadian system according to the model by Rea et al[11].

Table 1: **Illuminance and relative electrical power to achieve 50% melatonin suppression.** Several practical light sources with the photopic illuminance (lm/m^2) at the cornea required to achieve 50% melatonin suppression after one hour exposure. The relative electric power (W) need to achieve this same criterion response, based upon the current technologies, is also listed. Table 1 assumes 50% melatonin suppression for one hour exposure with a fixed pupil diameter of 2.3 mm).

Light Source	Illuminance(lux)	Relative Electric Power
2700 K compact fluorescent (Greenlite15WELS-M)	722	18
2856 K incandescent A lamp	511	75
3350 K linear fluorescent (GE F32T8 SP35)	501	10
4100 K linear fluorescent (GE F32T8 SP41)	708	14
5200 K LED phosphor white (Luxeon Star)	515	15
6220 K linear fluorescent (Philips Colortone 75)	349	12
8000 K Lumilux Skywhite fluorescent (OSI)	266	6
Blue LED (Luxeon Rebel, λ_{max} = 470 nm)	30	1
Daylight (CIE D65)	270	NA

Figure 2 illustrates the relative effectiveness of different light sources for stimulating the circadian system plotted as a function of photopic illuminance at the cornea. Also shown is a relative visual performance (RVP) response function.[21] Since the spectral sensitivity of the visual system as measured by RVP is well described by the photopic luminous efficiency function (Figure 1), the single RVP function characterizes visual performance for "white" light sources of different spectral irradiance functions, like those in Table 1.

Spatial Distribution

The effectiveness of light for the human circadian system cannot be determined from the spectral irradiance distribution alone. In contrast to the fundamental significance of optical refraction for image formation by the cornea and crystalline lens for the visual system, the circadian system appears to care little about the distribution of light across the retina. Although there is some evidence that the spatial sensitivity of the circadian system is not isotropic across the entire retina[22], it would seem that, as a first approximation, the circadian system responds simply to the total amount of circadian light incident on the retina. Light incident on the cornea will be, depending upon angle, differentially effective for entering the pupil and thereby stimulating the retinal mechanisms necessary for stimulating the circadian system. Using a ray-tracing technique, Van Derlofske et al. developed a spatial model of retinal irradiance that depends upon the angle of light incident on the cornea as occluded by the brow, cheek and nose (Figure 3). [23] Naturally, these complications vary with each person, but because they are limited to large entrance angles, the spatial sensitively of the retina appears to be closely approximated by a three-dimensional cosine distribution. According to this simpler model, the effectiveness of light incident on the cornea at increasingly eccentric angles falls off as the cosine from the optical axis of the pupil.

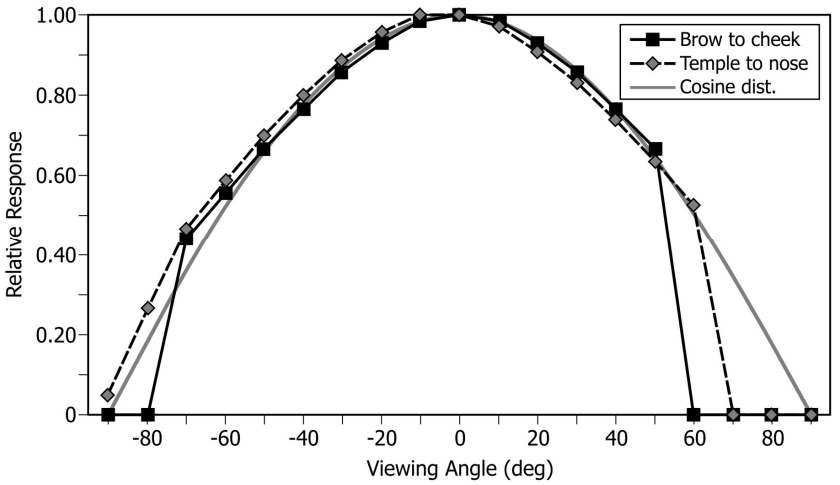

Figure 3: Spatial sensitivity of the left eye to light entering the pupil at different eccentricities from the optical axis (0 degrees) according to the model by Van Derlofsky et al.[23] As illustrated in this figure, the spatial sensitivity in the vertical plane (temple to nose) and in the horizontal plane (brow to cheek) closely follow a cosine distribution except at extreme angles.

Although this simple model is a useful first approximation of the spatial sensitivity of the circadian system, it will be increasingly important for the development of practical applications of circadian light that the distribution of neural phototransduction mechanisms underlying the circadian system in the retina be better understood. For

example, if the circadian system is more sensitive to light incident on the lower retina than the upper retina, as one study suggests[24], then lighting systems will need to be designed to deliver light to the cornea from above the normal viewing angle (e.g., an LED source mounted just above the computer screen).

Duration

The amount of time an individual is exposed to a light source must also be specified in order to predict the effect of light on the circadian system. Because the visual system is a remote sensing system and needs to respond to threats and opportunities very quickly, it will respond within a few hundred milliseconds to a briefly flashed or a moving target. In contrast, the circadian system appears to be quite slow to respond, if at all, to short duration flashes (like lightning flashes) and, apparently, not at all to moving light stimuli because of its coarse spatial sensitivity. Although little is known about the circadian system phase-shifting response to flashes of variable durations, the suppression of melatonin content in the bloodstream begins to respond after approximately two to ten minutes of sufficient light exposure. Based on studies conducted by McIntyre and colleagues[25], the amount of time required to achieve a criterion response by the circadian system will depend upon the duration of the light exposure. For example, 50% melatonin suppression by a "white" light (5500 K) at night took about 28 minutes following exposure to 3000 lx at the eye, about 33 minutes following exposure to 1000 lx at the eye, but 50% suppression could not be achieved following a 100 lx exposure level for any duration. Figure 4 illustrates the duration of light exposure needed to measure 50% nocturnal melatonin suppression by humans. [25]

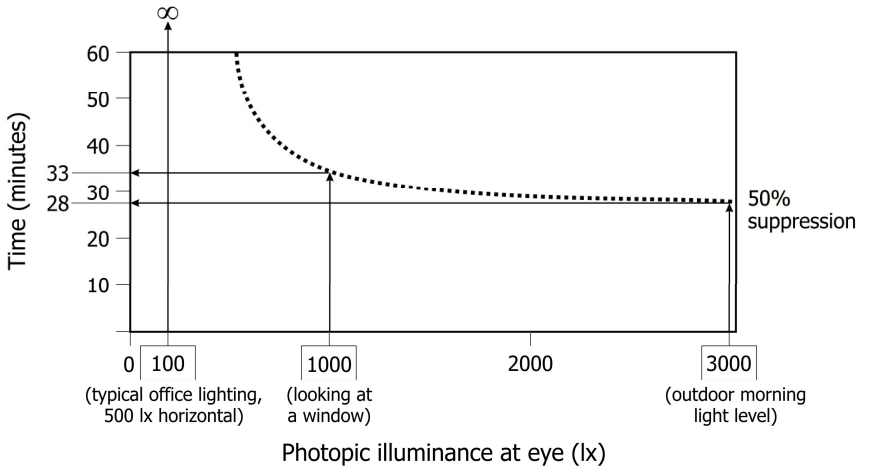

Figure 4: Duration of exposure, in minutes, to need to suppress nocturnal melatonin by 50% at different photopic illuminance levels (in lx), measured at the cornea, based upon McIntyre et al[25]. Typical illuminance levels one might experience during the day supplement the abscissa. Typical office lighting levels from white light sources (100 lx at the cornea) would not be sufficient to suppress nocturnal melatonin by 50% for any duration.

From a practical perspective, provision must be made for prolonged exposures to light (and to dark) for the circadian system to synchronize its operation to a 24-hour day.

Timing

Although the mechanisms are still unclear, the minimum amount of light needed for detection of light by the visual system changes only slightly over the 24-hour day.[26] Despite these slight changes, the visual system is essentially "ready to go" at any time of the day or night. In stark contrast, the response of the circadian system will change in the magnitude and in the direction of response depending on the timing of light exposure. Light can have a large or a small effect on the master clock and it can either phase advance or phase delay the clock depending upon *when* during the circadian cycle the retina was exposed to light. [27,28] Figure 5 illustrates this point.

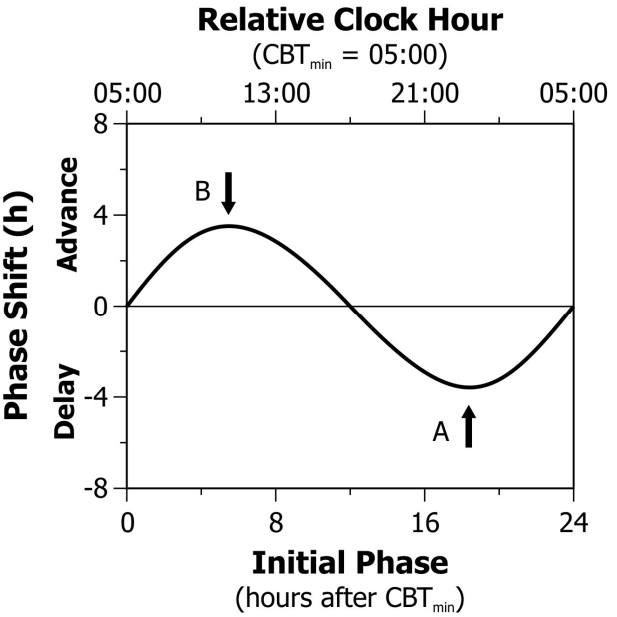

Figure 5: Human phase response curve (PRC) based upon Jewett et al[27] and Khalsa et al. [28] Light applied after minimum core body temperature (CBT_{min}) until mid-day (arrow B) will advance the phase of the master clock; light applied after mid-day and before CBT_{min} (arrow A) will delay the phase of the master clock.

Light-induced phase advances reset the master clock to an earlier time whereas delays will reset the clock to a later time. For example, if an otherwise synchronized person is exposed to light late at night, the master clock will tell the person to go to bed earlier and wake up earlier the following day (arrow B in Figure 5). However, if that same person is exposed to light in the early evening (arrow A in Figure 5) the clock will send information to go to bed later and wake up later the following day.

Because the typical period of the human biological clock is a bit longer than 24 hours, light in the morning upon awakening will advance the clock's timing every morning in order to keep biological functions synchronized with the solar day (e.g., arrow B in Figure 5). From a practical perspective then, sufficient morning light (quantity, spectrum, spatial distribution and duration) helps humans synchronize their lives to their diurnal schedules. The same evening light exposure will, however, delay bed times and rise times, potentially limiting sleep and compromising well-being. Understanding the timing of circadian light exposure is perhaps the most important characteristic to consider when developing new lighting technologies and applications.

History of light exposure on circadian systems

Finally, a word should be said about light history. Light exposures on preceding days and weeks influence the circadian system's current sensitivity to light. One study[29] demonstrated that, depending on the amount of light to which a laboratory animal was exposed in one part of the 24-hour day, dim light given in the other part of the day was interpreted by the circadian system as either light or dark. If the animal was alternately exposed to bright light and dim light for 12 hours each, the dim light was interpreted as the dark half of the light-dark cycle. If, however, the same animals were alternately exposed to the dim light and to darkness for 12 hours, the same dim light was interpreted as the light half of the light-dark cycle. In humans, the higher the exposure to light during the day, the lower the sensitivity of the circadian system to electric lights at night (e.g. Hebert et al.[30]). These findings in both animals and humans demonstrate that the circadian system responds to *changes* in the 24-hour light-dark cycle with less regard for the absolute levels.

From a practical perspective then, knowing an individual's history of light exposure is important for predicting the impact of light on, say, a farmer versus a computer programmer. Different lighting schemes may therefore have to be developed for the work place and for the home depending upon the individual's overall lifestyle.

Consequences and Implications

The human endogenous master clock has evolved to recognize a regularly occurring, 24-hour pattern of light and dark. There are, of course, genetic differences among individuals, so the coupling between the highly predictable 24-hour solar day and one's own internal clock will differ to some degree. For example, individuals can be characterized by what is termed their chronotype[31]; some people are *larks*, rising early in the day and going to bed early at night, while others are *owls*, going to bed late and, if they can, rising late in the morning. Interestingly, as individuals reach puberty, the propensity to become more owl-like increases until, when one reaches young adulthood, he or she returns to a more "normal" pattern of sleep-wake. [32] Toward the end of an individual's life, apoptosis begins to become problematic for many physiological systems, including circadian regulation. One begins to lose retinal neurons,

compromising not only the ability to see, but also the ability to register a robust daily pattern of light-dark that is needed to maintain entrainment. Individuals also lose neurons in the master clock itself, particularly in persons with Alzheimer's disease (AD)[33,34], further compromising our ability to synchronize both physiology and behavior to the 24-hour day.

Humans are a diurnal species, typically awake during the day and asleep at night. Thus, most vocations are performed during daylight hours, but nearly 15% of the US population are considered shift workers whereby they are active during the night and asleep during the day. [35] These people are rarely, however, true night-shift workers. Rather, most shift workers live a compromise between participation in a day-active society (friends, families, bank hours) and night-active employment. These people rarely have a regular, 24-hour light dark cycle. Epidemiological evidence indicates rather strongly that shift workers are more susceptible to obesity[36], cardiovascular disease[37] and cancers. [38]

As will be discussed, seniors are a population most likely to be positively affected by a prescribed 24-hour light/dark pattern. It is much more difficult to prescribe a light/dark pattern that will significantly improve sleep efficiency and alertness in rotating-shift workers. Little is known about the endogenous rhythms of rotating-shift workers, but more importantly, by definition for rotating shifts, they are going to experience aperiodic light/dark exposures. Consequently, rotating-shift workers are almost certainly not entrained to their work schedules and, as a result, experience symptoms similar to those experiencing "jet-lag" following trans-oceanic flights. Although high levels of light exposure during the night shift can increase acute alertness and reduce feelings of sleepiness[38,39], disruption of a regular 24-hour pattern of light and dark compromises entrainment. Moreover, acute suppression of nocturnal melatonin by high light levels at night has been linked to increased risk of cancer[40]. Therefore, it may simply be impossible to develop a prescribed lighting scheme for buildings where people work rotating shifts. It may be nevertheless possible to help minimize the problems associated with rotating-shift workers (poor sleep, poor performance, gastrointestinal disorders, obesity and breast cancer) by continuously controlling light/dark exposures on an individual basis. The science necessary for developing this interventional approach is just beginning, however, so no practical means of continuously controlling personal light/dark exposures are currently available for this purpose.

The combinations of genetic and environmental factors influencing circadian entrainment are infinite, so it is quite difficult to ascertain risk factors for a given individual and, moreover, to prescribe a "recipe" for minimal risk of disease on a personal level. It is possible, however, to identify populations who might be at risk and those populations where interventions would most likely be useful. The less that is known about the endogenous factors associated with circadian rhythms in a population or the less that is known about their exposures to light and to dark, the less likely it will be that successful corrective interventions will be implemented.

Lighting Schemes for Treating Circadian Sleep Disorders

Sleep disturbances in older adults are quite common**.** Seniors living in assisted living facilities are perhaps the best example population at risk of circadian disorders that could be alleviated by light treatment; due to age-dependent reduced retinal light exposures and to fixed lighting conditions in their living environments, seniors are less likely to experience the necessary, robust 24-hour, light/dark pattern needed for circadian entrainment. Prescribed 24-hour light/dark patterns have been shown to entrain circadian rhythms and thereby alleviate some sleep and agitation issues common among seniors, including those with AD. A 24-hour lighting scheme that delivers high circadian stimulation during the daytime hours, low circadian stimulation in the evening hours and night-lights that provide perceptual cues to decrease falls risks at night has been proposed.[41] Exposure to bright white light (at least 2500 lx and as high as 8000 lx at the cornea) for at least one hour in the morning for a period of at least two weeks was found to improve or consolidate nighttime sleep of AD patients. Greater sleep efficiency at night decreased the need to sleep during daytime hours and, in some cases, reduced agitated behavior such as pacing, aggressiveness, and speaking loudly.[42-46] Moreover, uncontrolled exposure to bright white light (average of 1136 lx at the cornea) during the entire day improved rest/activity of AD patients.[47] Finally, evening exposure to 30 lx of blue light from LEDs peaking at 470 nm at the eye for two hours consolidated rest/activity rhythms and increased sleep efficiency of older people with and without AD.[48,49] It is important to note, however, that a recent study failed to show significant improvement in nighttime sleep or daytime wake of AD patients after exposure to one hour of morning bright white light (>2500 lx at the eye).[50] Although seniors are more likely to benefit from light exposures, the application of light needs to be such that they are getting the correct dose at their corneas as well as getting the light at appropriate times. As discussed below, tuning the spectrum of light to optimally stimulate the circadian system will allow for use of lower light levels, reducing the likelihood of glare and increasing the likelihood of compliance.

Jet-lag is a temporary desynchronization between master clock time and environmental time (light/dark). The symptoms include insomnia and/or hypersomnia, fatigue, poor performance, and gastrointestinal problems. Eastward travel generally results in difficulty falling asleep, and westward travel results in difficulty maintaining sleep. Adaptation to a new time zone is usually slower after eastward travel than after westward travel. There are two main reasons for that: (1) those traveling east need to advance their biological clock to readjust to the local time at their destination; the time that daylight is available at the final destination will promote phase delay of the master clock and (2) it is easier for the timing of the biological clock to be delayed than advanced. One study[51] showed that a combination of advancing sleep schedules for one hour per day plus morning light treatment (½ hour of 5000 lx + half- hour of less than 60 lx at the cornea) for 3.5 hours advanced the phase of the biological clock, by 1.5 to 1.9 hours in three days. Although the principles for applying light treatment for reducing jet-lag symptoms are known, the

implementation of the light treatment may be a challenge. Airlines are starting to use colored light inside airplanes to improve mood, but it is probably very difficult to shift the circadian clock while one is inside the plane. Because the circadian clock is slow to shift, users need to start treatment a few days before they are scheduled to travel. However, because travelers have busy schedules, the likelihood of compliance is low. A personal light treatment device could be developed to increase the likelihood of compliance.

Delayed sleep phase disorder (DSPD) is a disorder of the timing of sleep; people suffering from DSPD typically go to bed late and wake up late (3 to 6 hours later than normal sleeping hours). This pattern interferes with people's normal functioning because they have difficulty waking up in the morning for work, school, and social obligations, and since they go to bed late, they do not sleep for as many hours as those going to bed at more normal hours. DSPD in adolescents is common and probably associated with hormonal changes that occur at puberty. The exact causes of DSPD are not actually known, but light exposure after minimum core body temperature and dim light during the evening have been shown to advance the phase of the master clock of persons with DSPD.[52] Using this information, two field studies[53,54] were very recently conducted to investigate the impact of light exposures on dim light melatonin onset (DLMO), a primary marker for the timing of the master clock, and on sleep duration for two populations of 8th graders. It was hypothesized for one study conducted in North Carolina that the lack of morning short-wavelength light (by wearing orange goggles) would delay the timing of the students' master clocks. For the other study conducted in New York, it was hypothesized that exposure to more evening light in spring relative to winter would also delay the master clocks of adolescents. In both studies, as expected, the students exhibited delayed DLMO as a result of removing short-wavelength morning light and as a result of seasonal changes in evening daylight. Also as expected, both sets of adolescents exhibited shorter sleep times; because of the delay in the timing of the master clock, they fell asleep later but still had to get up at a fixed time in the morning. These two field studies clearly demonstrate that by controlling circadian light exposures it is possible to practically and effectively control circadian time and thereby affect meaningful outcome measures like sleep duration.

Advanced sleep phase syndrome (ASPD) is another disorder of the timing of sleep, but unlike sufferers of DSPD, people with ASPD go to bed early and wake up early (3 to 6 hours earlier than normal sleeping hours). The cause of ASPD is still unknown, but it seems to be caused by genetic factors that result in a biological clock that runs with a period slightly shorter than 24 hours, instead of slightly greater than 24 hours, which is more normal. ASPD is a much less common disorder than DSPD. As with DSPD, using light as a treatment for this syndrome can help regulate and promote circadian entrainment. Light exposure in the early evening and reduced light during the morning has been shown to phase delay minimum core body temperature.[55]

Seasonal affective disorder (SAD) is a subtype of depression, with episodes occurring during winter months and remitting during summer months.[56] Symptoms of SAD include depression, hypersomnia, weight gain due to increased carbohydrate cravings, social withdrawal and even suicidal thoughts. It is believed that because daylight availability decreases in the winter at high latitudes, the number of people experiencing SAD increases as the latitude increases, affecting as much as 28% of the population living in places like Alaska. [56] "The winter blues" is a subtype of SAD and is even more common than SAD. The mechanisms of SAD are still unknown, and there are several competing hypotheses as to what causes SAD and how light can be used as a treatment. One of the competing hypotheses is that the late daybreak during winter months delays the circadian rhythms of those more susceptible to SAD; in this case, morning light is believed to be effective in treating symptoms of SAD. Another hypothesis is that the overall melatonin production of those suffering with SAD is greater during winter months than during summer months, which extends the amount of time during the 24-hour day that their bodies think it is nighttime; in this case, light in the early morning or evening is recommended. If a person is formally diagnosed with SAD by a general practitioner, insurance companies may pay for the cost of light treatment devices. A recent study[57] showed that 400 lx at the eye of blue light (λ_{max} = 470 nm) was able to significantly improve SAD symptoms compared to red light, which was used for placebo control. It has been suggested, however, that the positive impact of light on SAD symptoms is simply a result of placebo effects. Although research results may seem contradictory regarding its effectiveness, light treatment is still the most common non-pharmacological treatment prescribed for SAD.[58,59]

Lighting Devices for Treating Circadian Sleep Disorders

Light treatment has been successfully used to reduce symptoms of circadian sleep disorders described above. Light boxes using fluorescent light sources are the most common treatment devices available on the market. In general, light boxes provide a high amount of white light (2500 lx -10,000 lx at the cornea). The main disadvantages of such devices include the necessity to remain in one place for the duration of the treatment and the fact that some users experience discomfort from having to stare into the bright light. Until recently, light treatment devices used "full-spectrum" light. More recently, products have become available that use narrow-band blue (λ_{max} = 470 nm) and green (λ_{max} = 500 nm) LEDs. Because the circadian system is maximally sensitive to short wavelengths, much lower levels of blue and green light can be effective. The small, versatile nature of LEDs have also facilitated the development of personal light treatment devices, such as LED light goggles (Figure 6). Treatment devices such as these goggles can reduce the need to sit in front of a light box for extended periods of time and may lead to higher compliance in using light as a treatment option.

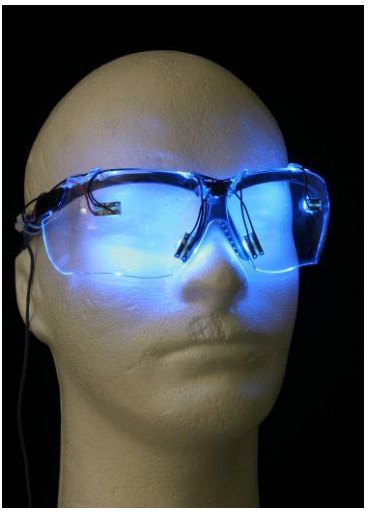

Figure 6: LED light goggles, such as these, are a treatment device that provides a customizable light therapy treatment. This new technology may replace light boxes as a light therapy treatment device in the future.

If compliance to light treatment devices is an issue, a dual ambient lighting scheme that maximizes circadian stimulation during the day (bright, bluish-white light) and minimizes it at night (dim, yellowish-white light), while maintaining good visibility at any time. This approach has been proposed for older adults' residences.[39] The ability to control the light level and spectrum is very important when it comes to providing good circadian lighting without compromising the visual requirements for seniors.

Dawn simulators are marketed primarily for people with seasonal depression; these devices are programmed to gradually increase the light levels in the morning hours, simulating the sunrise. While the evidence of effectiveness is limited, and light quantities achieved are often below those from other light treatment devices, dawn simulators may have therapeutic value for certain sleep disorders and might serve as a supplement to other light treatment strategies. To accurately assess the efficacy for any light treatment method, however, it is necessary to measure circadian light exposure throughout waking hours.

A low-cost alternative to commercial products would be for people to spend 20-30 minutes outdoors daily, preferably at about the same time each morning. Even an overcast day will produce 2500 lx at the cornea, and bright sunshine can produce exposures greater than 10,000 lx at the cornea.

It should be noted that removing circadian light at certain times is just as important as being exposed to circadian light at other times; therefore, the use of personal light treatment devices that provide and remove short-wavelength light based on each

individual's desired entrainment schedule is envisioned. The use of the Daysimeter[60], a circadian and photopic light meter, can be used together with a feedback control system that will let the user know when to receive and when to remove circadian light to maintain or adjust entrainment. Currently, all light treatment devices and prescriptions are effectively "open loop" control systems, which mean that light is given at a prescribed clock time (i.e., morning or evening) without respect to the person's own internal clock or without respect to unexpected light exposures. An exciting prospect for personal lighting control systems to increase effectiveness of light treatment will be the development of "closed loop" feedback systems that assure that light and dark are being delivered according to an individual's circadian time in the context of unexpected light exposures experienced in normal life activities.

Summary

This overview of the impact of light on the circadian system and its effects on our health and well-being underscores the importance of developing a new definition of circadian light as well as a new framework for lighting practice whereby those lighting characteristics that affect the visual system are integrated with those lighting characteristics that affect the circadian system. Because there are great differences between the visual and circadian systems' responses to the quantity of light, its spectral composition, spatial distribution, timing, and duration, generalizations about "quality lighting" will have to be assessed by two very different sets of criteria in the future. Although the information and recommendations presented here will certainly be refined as more research is undertaken, little progress will be made in delivering "healthy lighting" to society until researchers and practitioners begin to consider, measure, calculate, and control the fundamental characteristics of light for the circadian system, not just for the visual system. This chapter was intended to serve as a step toward that goal.

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