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A review of the effect of colour and light on non-image function in humans

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Abstract

This paper reviews the non-image forming aspect of vision. Developments in the last twenty years have seen the discovery of a fifth class of human visual pigment (melanopsin) in addition to the three classes of photopsins in the cones and rhodopsin in the rods. Melanopsin is found in a small number of retinal ganglion cells which then, in addition to receiving input from the rods and cones, are intrinsically photosensitive. These intrinsically photosensitive retinal ganglion cells send their input primarily to the hypothalamus where they help to regulate the circadian system (daily rhythms of sleeping patterns, body temperature, heart rate etc.). The discovery of the anatomical basis of non-image forming vision has led to a great deal of research into the effects of light on sleep, depression and mood, retinal photodamage, and wellbeing, amongst other topics. Given the recent technological innovations in LED lighting that now give us greater control over our environmental lighting it is timely to review the non-visual effects of light on humans to inform lighting design in the future.

Introduction

It is now known that the eyes perform two functions: image-forming (IF) and non-image-forming (NIF) vision. Whereas the IF visual system allows us to see and is primarily mediated by the cones and four classes of photoreceptors (three photopsins in the cones and rhodopsin in the rods), the NIF function of the eye is primarily activated by a fifth photopigment, melanopsin, which is found in the retinal ganglion cells in the retina (though a different layer in the retina than that where the rods and cones are located). Whereas the rods and cones mainly send signals via the laterate geniculate nuclei to the back of the brain (specifically, the visual cortex) retinal ganglion cells that contain melanopsin transmit signals to the hypothalamus where they help to regulate the circadian system that controls, amongst other things, our sleeping and waking periods. Given the increased interest in the effect of light and colour on aspects of human performance beyond vision, the progress that has recently been made in understanding the NIF visual system, and the technological innovations that now give us greater control over our environmental lighting at home and in the workplace, it is timely to review the non-visual effects of light on humans.

Table 1: Organisation of the review and a list of the effects that are included.

Circadian Disruption and entrainment	Age-Related Macular Degeneration	Mood and Wellbeing	Cancer	Other Medical Effects	Heart Rate and Blood Pressure	Reading, Autism and Headaches	Office and Learning Environments
Sleep disorders	blindness	Seasonal Affective Disorder	Skin damage	Wound treatment	Heart rate	Meares-Irlen syndrome	Preference
Melatonin suppression	Retinal damage	Mood	Skin and breast tumours	Burn treatment	Blood pressure	Dyslexia	Impulsivity, reaction times, and creativity
Alertness		Colour Emotion	Colorectal cancer	Tinnitus	Skin conductance	Migraine	Flicker
Mood and Wellbeing				Vestibular dysfunction		Autism	Alertness and attention Dynamic lighting Relaxation Headaches and eyestrain Problem solving and performance

In this review paper a summary is first given of the NIF visual system and its relationship with the more widely understood IF visual system. Afterwards the literature available on the effect of light and colour on health issues and on performance is reviewed. Under health issues the

topics discussed are sleep and alertness, age-related macular degeneration, cancer, anti-bacterial activity, heart rate and blood pressure, and reading, learning and other disorders. Under performance issues the topics discussed are learning and productivity, impulsivity and creativity, jet lag, and mood and wellbeing. The material is presented under several headings and Table 1 summarises these and lists all of the effects that are included in this review.

The IF and NIF Visual Responses

Human colour vision is mediated by three classes of light-sensitive cones that each have broad-band spectral sensitivity but with peak sensitivities at the short (420 nm), medium (530 nm) and long (560 nm) wavelength. The cones are active under so-called photopic levels of illumination. At lower levels (scotopic) the cones are unresponsive and human vision is mediated by the rods which have peak sensitivity at about 498 nm. Under photopic conditions colour vision results from two opponent processes alongside a luminance response. The yellow-blue opponent system is common in species with dichromatic vision. In evolutionary terms the yellow-blue system is thought to be as many as 800 million years old whereas the red-green opponent system evolved much later, perhaps 40 million years ago, in Old World Monkeys [1]. Today, humans and Old World Monkeys are unique in being trichromats with the majority of mammals being dichromats whereas most birds and fish are tetrachromats.

The notion of trichromacy in humans was postulated in the 19th Century by Thomas Young and is the basis, of course, of the CIE system that was developed in 1931 [2] although actual measurements of the photopigments in humans were not confirmed until the second half of the 20th Century [3-4]. The rods and cones are located in the retina and generate signals that in turn activate the bipolar layer of cells which then activate the retinal ganglion cells whose signals leave the eye via the optic nerve. Whereas most humans are trichromatic a small number of people are dichromatic and possess colour-defective vision [5]. However, more recently it has been determined that some females are tetrachromatic [6].

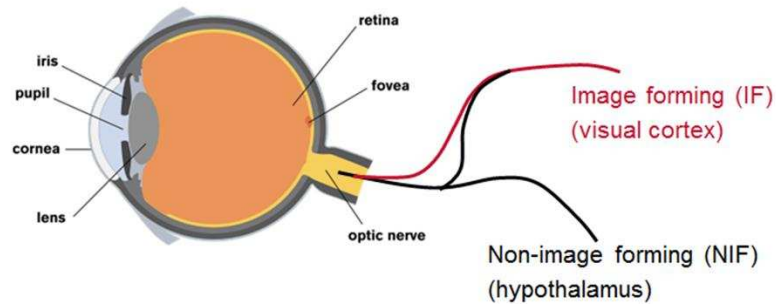


Figure 1: Schematic diagram to show the image-forming (IF) and non-image-forming (NIF) visual systems. As shown the two systems may not exist in isolation but may interact with each other.

Until the late part of the 20th the retina in trichromatic human observers was assumed to contain four photopigments and IF vision was thought to be the only function of the eyes. The three cone-based photopigments in humans are based on the protein photopsin and the rod-based photopigment is based on the protein rhodopsin. A fifth human photopigment, based on the protein melanopsin, was discovered in humans at the turn of the century [7-8] after being earlier found in frogs and mice [9]. Melanopsin is found in some retinal ganglion cells which then are intrinsically photosensitive (in addition, the retinal ganglion cells are responsive to light by the normal route of receiving signals from the rods and cones via the bipolar cells). Intrinsically photosensitive retinal ganglion cells (ipRGC) mainly send their output to the suprachiasmatic nuclei of the hypothalamus (the so-called retinohypothalamic tract) whereas the rods and cones send their signals to the visual cortex via the lateral geniculate nuclei. We now know that the eyes – like the ears that give us the twin functions of hearing and balance - perform two functions, IF vision and NIF vision (see Figure 1). The ipRGCs are primarily responsible for this NIF function, regulating the circadian system – the cycle that is approximately 24 hours and which controls our sleep and waking periods - but are also known to regulate pupil size. The existence of a diurnal cycle was first discovered in 1958 with plankton [10] but was not thought to exist in humans in a way that is entrained by light until much later [11].

However, it may not be so straight forward that the rods and cones contribute towards IF vision and the ipRGC contribute towards the NIF system [12]. For example, under low light condition the rods can regulate the circadian system and the ipRGC cells may contribute

towards IF vision [12]. Mice without functioning rods and cones have been shown to be able to discriminate between spatial patterns in visual tests [13]. The ipRGCs combine input from the rods and cones with their own, more sluggish, melanopsin-mediated response to transmit signals to various regions of the brain involved in both IF and NIF vision [14].

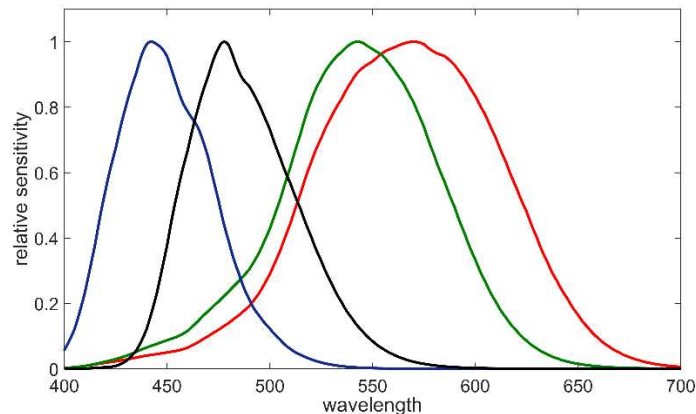


Figure 2: The relative spectral sensitivity of the cones (from Stockman and Sharpe, 2000 [19]) and the photopigment melanopsin [15] which is found in the intrinsically photosensitive retinal ganglion cells.

Melanopsin is the fifth photopigment in humans and has a peak absorbance at about 480 nm (see Figure 2) [15]. Like the photopigments in the rods and cones, it is isomerised on light absorption, converting 11-*cis* retinal to all-*trans* retinal [16] although it may regenerate by a different mechanism than that which has been established for the rod and cone photopigments [9]. The human retina contains about 120 million rods and 6 million cones; by contrast there are only about 3000 ipRGCs [9]. Cones can respond to temporal modulations in luminance of 100-200 ms [17]; by contrast, the response of ipRGCs has a slow onset and sustained depolarisation that can last for as long as 30 s after the light is turned off [14]. Despite the fact that melanopsin can respond to a single photon of light it is less sensitive than the photopigments in the rods and cones; it is believed that this is because there is a low probability of photon capture [14]. It is now established that retinal light exposure elicits nonvisual responses in humans, including modulation of alertness and cognition [18-20].

This paper reviews the effect of light on aspects of human performance beyond colour vision. It is not clear, in many cases, whether these effects are the result of the IF or the NIF visual function of the eye (that is, the cones or the ipRGCs) or both.

Circadian Entrainment and Disruption

In the USA approximately 30% of working adults average less than 6 hours sleep per night but 50 years ago only 3% of the working population slept so little [22]. Poor sleep is associated with greater risk of obesity, diabetes, heart disease, depression and stroke [23]. One factor in the change in sleep patterns in society may be increased use of light. Between 1950 and 2000 the cost of light fell six-fold but our usage per capita rose fourfold [22]. Use and control of light is increasingly being considered as a non-drug alternative to alleviate age-related sleep disturbance [24]. Light has been shown to exert strong alerting effects that depend upon several parameters such as irradiance, duration, the time of day of exposure, and the spectral composition of the light [25-26].

In the morning when we wake, the secretion of the hormone melatonin by the pineal gland is inhibited and the adrenal gland secretes cortisol (a hormone that is produced in large quantities when we are stressed but which is also, like melatonin, part of the circadian cycle). Melatonin starts rising about 2 hours prior to natural bedtime [27] and is involved in the circadian rhythms of several physiological functions including sleep timing and blood-pressure regulation [28]. Activation of the ipRGC by light after dusk inhibits sleep-promoting neurons, activates arousal-promoting neurons in the hypothalamus, and inhibits the secretion of melatonin. Light at night disrupts the circadian system, interferes with our sleep and increases alertness [22]. Measurements of brain responses using fMRI have shown greater responses in the hippocampus to blue light rather than green light [18]. Blue light is most problematic because of the spectral sensitivity of the photopigment melanopsin (Figure 2). Measurement of melatonin levels in the body (usually from saliva samples) are therefore often used as a measure of alertness in various experimental paradigms. Today's lighting environment has substantially changed from that experienced during evolution; in most parts of the world artificial light has replaced natural sunlight during the day and artificial light at night has replaced darkness [29]. Reduction in sleep and the associated lowering of melatonin levels is associated with a great number of other illnesses including cancer, heart disease and mental health [22, 30-31].

The ability of light to disrupt the circadian system and suppress levels of melatonin was established before the discovery of the ipRGCs in humans in 2002 [32-34]. However, over the

last decade or so the role of the NIF visual system in this process has become better understood. The spectral sensitivity of the ability of light to suppress nocturnal melatonin in humans has been investigated and action spectra constructed that show distinct short-wavelength sensitivity peaking between 460 nm and 490 nm [35-36]. An interesting study was conducted with participants at a polar base station (where there is no access to sunlight in winter) and where sleep problems and circadian misalignment are often reported [37]. A combination of melatonin-level measurement (from saliva samples) and self-reporting was used to assess the effect of standard fluorescent white lights and blue-enriched lights in the daytime and it was found that the blue-enriched light resulted in substantially less delay in the onset of melatonin in the evening. In another study participants underwent continuous EEG recordings and undertook a series of tests whilst exposed to 555 nm light or 460 nm light [38]; under the blue light participants had lower subjective sleepiness and increased EEG alpha waves. Significantly less melatonin suppression has been noted in elderly subjects compared with young subjects and this may result from age-related changes in lens density in the eye [39]. This means that younger people may be at particular risk from using artificial light at night.

Although the primary concern is about the use of light in the home, there is some concern that evening use of emissive displays (smart phones and tablets) is partly responsible for the changing sleep patterns that have been observed [40]. Figure 3 shows the spectral emissions of two popular smart phones when white is displayed and it is clear that there is substantial radiation in the region where the NIF system is sensitive. Although there is a great deal of speculation about the negative impact of using mobile displays at night, it is likely that the increased use of room lighting at home (and the replacement of warm Tungsten light bulbs that had low intensity in the potentially harmful short wavelengths) is an even greater problem. A recent study found that exposure to bright room light (200 lux) suppressed melatonin and resulted in later melatonin onset compared with a dim light (less than 3 lux) condition [41]. Evening light levels at home as low as 65 lux can alter circadian timing [42].

In terms of colour, 420 nm has a stronger effect than 470 nm which in turn is more effective than 600 nm [43]. However, light at 460 nm was found to significantly suppress melatonin levels to a greater extent than light at 420 nm [44]. In a study about daytime sleeping, green

light at 500 nm (administered via a light mask) was not found to inhibit sleep [45]. There is some suggestion that adolescents may be more sensitive than adults and that they could be at particular risk from blue light. Use of self-luminous devices for 1 or 2 hours prior to natural bedtime reduced melatonin levels in adolescents by 23% and 38% respectively [27].

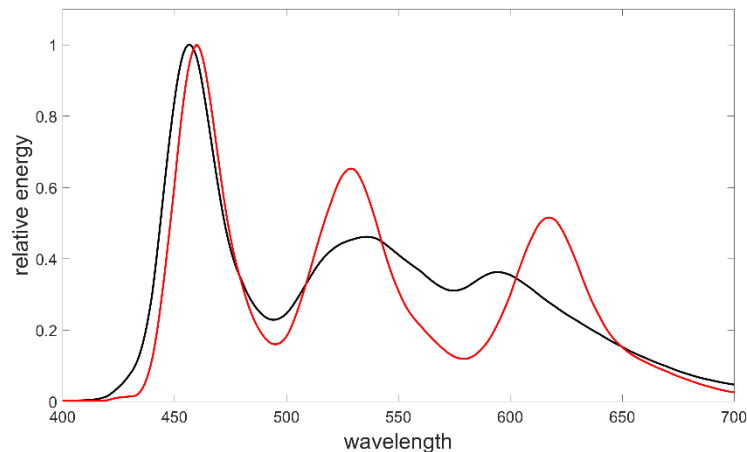


Figure 3: The relative spectral emissions from two commercial smartphones when white is displayed demonstrating that both devices emit substantial short-wavelength light.

Although blue light late at night is problematic, during the day a high colour temperature (and high intensity) of lighting is actually required for synchronisation of the circadian system [46]. A study of elderly patients with insomnia found that exposure to bright light in the early evening was beneficial [24]. The effect of bright light at lunchtime in a geriatric hospital resulted in clinical improvements in sleep and wakefulness [47]. Light at a correlated colour temperature (CCT) of 6500K (40 lux for 2 hours in the evening) significantly increased alertness and suppressed melatonin levels compared with light at 2500K [48]. The correlated colour temperature is a measure of the colour of light sources by referring to the closest point in CIE chromaticity space on the blackbody locus (see Figure 4). Office workers exposed to either a blue-enriched light (17000K) or a white light (4000K) showed increased alertness and positive mood, and decreased evening fatigue, after exposure to the blue-enriched light as measured subjectively when compared with the white light [49]. In a similar study, but with subjects who were sleep deprived, a dawn-simulating light (gradually increasing from 0 to 250 lux) in the morning resulted in enhanced mood and well-being compared with use of a blue light (100 lux at 470 nm) [50]. Light can also have other positive effects; for example, sunlight acts via the skin for the synthesis of vitamin D [51].

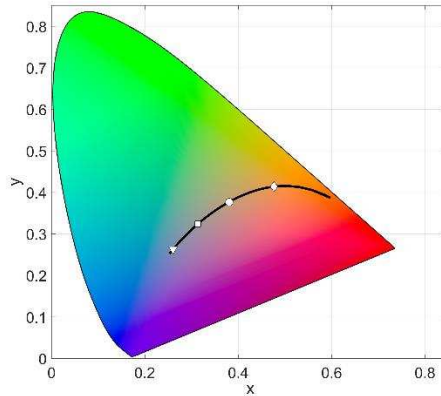


Figure 4: CIE chromaticity diagram showing the blackbody locus (solid line) and the chromaticities of lights with a colour temperature of 2500K (diamond symbol), 4000k (circle symbol), 6500K (square symbol), and 17000K (triangle symbol).

Some questions still remain. Most studies link the alerting effects of light to its ability to suppress melatonin but in at least one study both short (blue) and long (red) wavelengths were found to increase alertness in the night after a period of darkness although only the short-wavelength light significantly suppressed melatonin levels [52]. It has been noted that the relative contribution of rods, cones and ipRGC to NIF responses under light conditions differing in irradiance, duration, and spectral composition remains to be determined in humans [53]. In one study subjects were exposed to blue (460 nm) or green (555 nm) light near the onset of nocturnal melatonin secretion; at the beginning both lights were equally effective but spectral sensitivity to 555 nm light decayed exponentially suggesting a significant contribution of cones to NIF vision at the beginning of the light exposure [54]. A study with subjects who had been deprived of quality sleep for two consecutive nights found no difference between the effects of two lights (one of which was much richer in short wavelengths) on subjective alertness, energy and mood suggesting that when sleepiness is high the ability of classical photoreceptors to increase alertness cannot be ruled out [55]. It has also been reported that in mice blue light causes an increase in alertness whereas green light promotes sleep [26]. In another study, it has been shown that light can be used to increase alertness in the afternoon but that red light is a stronger alerting stimulus than blue light [56].

Another interesting effect of light is in the alleviation of the effects of jet lag, which results from the temporary loss of synchrony between an abruptly shifted sleep period, timed in

accordance with the new local day-night cycle, and a gradually re-entraining circadian system. Jet lag is often confused with travel fatigue, but the symptoms do not disappear after a good night's sleep [57]. The most commonly experienced symptoms are sleep disorders, difficulties with concentrating, irritability, depression, fatigue, disorientation, loss of appetite, and gastrointestinal disturbance [58]. For short stop overs adapting the circadian system is not advised even if it were possible but for longer stays strategies to hasten adaptation include exposure to, and avoidance of, light [59]. However, the published research has produced inconclusive evidence so far.

In the 1990s laboratory simulations, in which sleep was advanced 6-8 hours and subjects exposed to 3-4 hours of bright light for several days, were not at all conclusive [60]. One possible reason for this is that jet lag is associated with other factors such as stress and tiredness in addition to the time shift and therefore the simulations do not replicate real-world conditions. In one early study in a realistic setting, four subjects underwent light treatment before and after a flight from Tokyo to San Francisco; two of them received 3 hours of bright light at 11 am (San Francisco time) for three days after arrival and showed enhanced sleep efficiency compared with the other two who received dim light treatment [61]. However, in a later study with 20 subjects who flew from Zurich to New York light treatment showed significantly larger phase delays in melatonin onset but little behavioural benefit [62]. These studies are promising but limited due to the relatively small sample size. A review of the literature concluded that laboratory studies do not unequivocally support the hypothesis that bright light alleviates jet lag and the sparse number of field studies do not allow a clear judgment on the beneficial effect of bright light treatment on jet lag [63].

Most studies have looked at light treatment after arrival in a new time zone. However, one study considered the use of light treatment to advance their circadian rhythms prior to travelling eastwards and found greater (though not statistically significant) advancement with bright light than with dim light [64]. Although not directly related to jet lag an interesting study looked at the psychological and physiological indicators of time perception when subjects were exposed to various monochromatic light environments [65]. The psychological indicators showed that time was perceived to run faster in red light than in any other coloured light and there was some support from the EEG measurements that were also taken.

Age-Related Macular Degeneration

Age-related macular degeneration (AMD) is the leading cause of irreversible blindness in the developed world and usually affects people over 50 years of age [66]. It is ironic that the very light that we require to see is highly damaging to our visual systems. AMD is caused by damage to the macula of the retina and results in blurred vision or, in extreme cases, no vision at all in the centre of the visual field (see Figure 5). The macula is the central area of the retina which contains the highest density of photoreceptors and is responsible for high-resolution spatial acuity. The photoreceptors are susceptible to damage by light, particularly short-wavelength light [67-68]; free retinal (an essential element in the photochemical process of vision) is phototoxic [69]. Short-wavelength light is a particular threat because the photons at this wavelength are high energy and have the power to damage the cellular structure and function of photoreceptors [69]. Blue light has been described as 50-80 times more effective at causing photoreceptor damage [70]. Most ultraviolet radiation below 295 nm is blocked by the cornea whereas much of the UV-A (315-400 nm) and UV-B (280-315 nm) light is absorbed by the lens. However, some radiation lower than 400 nm does reach the retina [69]. The macula area is naturally yellow due to the presence of various xanthophyll carotenoids (such as lutein) which may give protection against blue light [68] and are also free-radical scavengers [69]. The lutein or macula pigment has been described as 'nature's notch pigment' [71].

It has long been suggested that exposure to blue and white light (especially in later life) could be a contributory factor in AMD [72] although much of the research has been based on animal experiments. Experiments with rats, for example, have found photoreceptor apoptosis after exposure to 400-480 nm light [73]. Using narrowband radiation blue (403 nm) light was found to severely damage rat photoreceptors whereas green (550 nm) of the same energy did not [74]. However, animal data and models may not be relevant for human pathology [75]. A review in 2004 suggested that the evidence suggests, but does not yet confirm, that blue light is a risk factor for AMD in humans [76]. More recently, it has been suggested that eye protection should be worn in very bright outdoor conditions to protect against the risk of ADM [77].



Figure 5: An image to simulate what vision is like for someone with moderate AMD (image reproduced with permission from <http://www.inclusivedesigntoolkit.com/betterdesign2/simsoftware/simsoftware.html>).

The European Union phased out the sale of incandescent light bulbs over the last ten years and it has been estimated that if white LEDs replace all other light sources about 270 million tons of CO₂ per year would be saved [76]. However, the replacement of Tungsten light with LED lights that are rich in short-wavelength light represents a potential health hazard. Disruption of circadian rhythm, loss of sleep, and early onset of AMD are three serious risks that could be increased with the increased use of light (and blue light in particular) in our homes and workplaces. A recent review by the French Agency for Food, Environmental and Occupational Health and Safety noted that serious effects of chronic day-long life-time exposure to blue light could not be ruled out [75]. In a 2014 study albino rats subject to illumination by white LEDs to simulate typical domestic light showed evidence of retinal damage and cell death after just 9 days of exposure [78]. Blue light is not without virtue however [79]. Indoor light that is deficient in short-wavelength light may be detrimental for myopia [80] and is required during the day for entrainment of the circadian system. Insufficient blue light during the day can also negatively affect mood and lead to depression [81].

Mood and Wellbeing

There is a long history of research that shows that colour can have an effect on mood [82-83]. A huge number of publications now exist on this topic and these are not fully included in this review since most of that research is arguably about the visual effects of colour. However, a very brief overview of some ideas in colour emotion is presented in this section along with some effects that may likely be associated with the NIF visual process and seasonal affective disorder.

Colours have strong associations and can affect mood and emotion. Many associations [84] are almost certainly the result of the IF visual process and fall outside the remit of this paper; however, it is not clear whether the emotional effect of colour is the result of the IF or NIF visual system. The effect of colour and light on emotion has been referred to in the recent literature as colour emotion [85-88] although there is some confusion in the literature between the emotional effect of a colour and a simple association of colour with a concept or idea. Much of the recent research in colour emotion uses scaling techniques to assign colours to bi-polar scales such as masculine-feminine or warm-cold. Some work has attempted to find principal factors or dimensions for colour emotion. For example, Kobayashi developed three main dimensions of colour emotions: warm-cool, soft-hard and clear-greyish [10] and Sato *et al.* found the dimensions to be warm-cool, potency and activity which were found to be associated with the colour-appearance attributes, hue, lightness and chroma [11]. More recently, Ou and Luo and co-workers have developed models for single and two-colour stimuli and have discussed the relationship between colour emotion and colour preference [85-87].

Some studies have found that mood in a living or workplace environment can be affected by colour [89] although others have found that environmental colour has no effect on mood [90, 91]. A study was conducted in a light laboratory to simulate perceptions of participants in an aircraft cabin when exposed to different lighting situations [92]. It was found that room temperature was perceived as being different depending on the colour of the lighting; in yellow light, room temperature was felt to be warmer than in blue light. Subjects felt more alert in blue light. There is currently great interest in dynamic lighting and its effect on mood and perception [93].

There is some evidence that performance and mood are adversely affected by non-visual flicker in some fluorescent lights [94]. In office environments, subjects reported a more positive mood under 2000 than under 300 lux [95]. In countries north of the equator there was significant variation in mood over the year that did not occur with countries closer to the equator; mood was lowest when it was dark but there was an optimal brightness where mood was found to be best [83].

Seasonal affective disorder (SAD) is a form of recurrent depressive or bipolar disorder, with episodes that vary in severity and normally occur annually [81, 96]. Most cases are associated with winter depression and are thought to be aggravated by low light levels although SAD cases associated with other seasons (such as summer depression) are also noted [81]. For winter-based SAD exposure to light in the morning is a common treatment and preliminary experiments with light were carried out in the 1980s [81, 97-98]. It was suggested that an effective treatment (usually measured by improvements in the Hamilton Rating Scale for Depression) should include 2500 lux of artificial light exposure in the morning at least twice daily for one week [99]. Early treatments were affected using a viewing cabinet fitted with a 4000K fluorescent tube [100]. Illumination of different areas of the human retina generates different amounts of melatonin suppression [101]. Such findings suggest that a non-homogenous distribution of ipRGC cells in the human retina so that the geometric relationship of any lighting with the observer may be an important factor. The use of a light above eye level with the eyes looking downwards towards a work surface is supported by studies that show enhancement of melatonin suppression with directional illumination of the lower retina [101]. Currently there is interest in light-emissive visors known as dawn simulators that can mimic the gradual twilight transitions found outdoors naturally [100].

Although initial treatments used broadband white light an increased understanding of the NIF visual process has led to interest in treatments with shorter wavelengths but studies that have been reported have produced quite contradictory findings. One early study found that white light was more effective than either red or blue light [102] and another suggested that broadband white light was more effective than green light [103]. A further study found that green light is a more effective treatment than red light [104]. Both bright white light and dim red light were also found to be effective with no statistical difference between them [105]. In

a later study narrowband blue light (468 nm) from LEDs was shown to be more effective than red light (654 nm) although in this study the red light was also dimmer than the blue light [106]. The inclusion of UV-A wavelengths in the treatment has been shown to be ineffective [107]. Since the 1990s it became common for 10,000 lux to be the recommended treatment [108] although it has also been suggested that the recommended dose may be too high if narrowband short-wavelength light is used [109]. Some mild side effects of light treatment have been reported including headaches, eye strain and feeling 'wired' [107-108].

The slightly confusing picture about whether short-wavelength light is more effective than broadband white light may have arisen because the relative contributions of the cones, rods and the ipRGCs to NIF visual function may depend upon various parameters such as illuminance level, time of day and duration. Many published studies about light therapy for mood disorders failed to meet certain criteria but a meta-analysis of published studies that did meet these criteria concluded that bright light is effective with an efficacy equivalent to anti-depressant drugs [110]. It is less clear that light therapy is an effective treatment for non-seasonal depression but some efficacy has been noted when used in conjunction with anti-depressants [111-112]. Some effect of light treatment has also been found in treatment of cases of bulimia nervosa that are worsened in winter [113-114] and elderly dementia [112].

Cancer

The most familiar human photochemical damage is skin cancer [115]. Ultraviolet radiation in sunlight is the most prominent and ubiquitous physical carcinogen in our natural environment [116] but does not penetrate deeper than the skin. The relationship between skin cancer and sun exposure was suspected in the late 19th Century and confirmed experimentally in the early part of the 20th Century [116]. Both UV-A (315-400 nm) and UV-B (280-315 nm) radiation play an important role in conditions such as premature skin ageing, eye damage (including cataracts) and skin cancers [117]. Some concern has been expressed that indoor lighting could be harmful. Compact fluorescent lamps could result in overexposure of the skin by UV light when used in desk or task-lighting applications [118] although this has recently been

contested [119-120]. Other researchers have argued that TVs, tablets and computers pose no UV risk to humans when used at a safe distance [121].

In addition to cancer there is also the possibility that UV, visible and infrared radiation can cause skin damage [122]. Visible and infrared radiation can raise the temperature of skin (and of the cornea of the eye) and if the temperature elevation is sufficient it can produce burning. The Illuminating Engineering Society of North America Recommended Practice 27 has set out a system for classifying light sources according to the level of radiation risk they represent [122]. Meanwhile the Commission Internationale de L'Eclairage has published a biological safety standard that may be used to assess LED lighting [123].

There has been some suggestion that exposure to blue light, in particular, during the late evening or at night could be a cancer risk by reducing the amount of melatonin in the body. A number of animal studies have shown that melatonin is effective against cancer. It is a powerful anti-oxidant and free radical scavenger. For example, in hundreds of investigations, melatonin has been documented to ameliorate the oxidative injuries in tissue due to ionizing radiation [124]. It is beyond doubt that melatonin has significant atoxic, apoptotic, oncostatic, angiogenetic, differentiating and anti-proliferative properties against all solid and liquid tumours [125]. It has also long been known that there is a higher risk of breast cancer in industrialised societies than in non-industrialised areas [126]. Since exposure to light at night can decrease production of melatonin by the pineal gland, and melatonin has been shown to suppress mammary tumorigenesis in some animals, it was suggested that the use of light at night (and hence night shift work itself) could be a contributory factor for the high rates of breast cancer in industrialised areas. Some studies have suggested that light at night may be associated with the risk of developing breast cancer in humans [127-128] and that nurses who work night shifts may have greater risk of colorectal cancer [129]. Indeed, a World Health Organisation review concluded that shift work involving circadian disruption is probably carcinogenic to humans [130]. Recently, however, a meta-analysis of seven studies (involving 1.4 million women in total) looked at shift work and incidence of cancer and concluded that night shift work has little or no effect on breast cancer incidence [131].

Heart Rate and Blood Pressure

Although much of the popular media assumes that colour affects heart rate and blood pressure, a review in 1984 found inconclusive data [132]. However, Kaiser noted one study in which systolic blood pressure was higher when observers viewed the colour red than white and that these responses were higher than for blue but this was in an unpublished PhD thesis in 1958 [133]. It is known, nevertheless, from studies with rats that the heart is under control of the suprachiasmatic nucleus (which is at the centre of the circadian system) and in humans there is a time-of-day-dependent simulation of resting heart rate by moderate light intensities [134-135]; typically, the heart rate is about 6 beats per minute faster at noon than during sleep. Experiments have shown that bursts of bright light can raise heart rate compared with the resting heart rate in the dark [135]. Illumination at 1000 lux has also been shown to increase heart rate compared with similarly coloured (4000K) illumination at 250 lux [136].

A number of new studies using coloured light and environments have been carried out since 1984. A study with 60 participants exposed to red, white and blue light found no differential effect of light colour on heart rate or skin conductance [137]. A later study found that participants blood pressure fell when they relaxed in a pink room but it was not fully controlled so that, for example, blood pressure, may have also fallen had the participants relaxed in a white room [138]. Recently, study participants were placed in a coloured lighting environment and it was found that, relative to the white condition, heart rate increased in the red condition and decreased in the blue and in the green conditions; however, the effects were not statistically significant [139]. Recently, in a study where students were presented with differently coloured learning environments, heart rate was increased for red and yellow and decreased for blue with the effects being significant [140]. In a sleep study participants were exposed to light during the late evening and light at 460 nm led to significantly higher heart rates than light at 550 nm (or the no-light control condition) [25]. However, whereas the effect of light intensity on heart rate is quite well established, over 30 years since Kaiser's 1984 review the evidence for an effect of colour (whether light or environment) on heart rate

and blood pressure is still not entirely convincing and more work is needed for a definitive conclusion.

Reading/Learning Disorders, Autism and Headaches

Some people experience stress and headaches whilst reading (Meares-Irlen syndrome) and about 375,000 children in the UK have dyslexia [141]. It has long been believed that the use of coloured overlays can reduce the distortion experienced by children with reading difficulties (and others who suffer from eye strain) and alleviate symptoms although different colours are most effective for different people [142-143]. The rate of reading (assessed using the Wilkins Rate of Reading Test) for some participants with learning difficulty was found to be significantly faster when using a coloured overlay [144]. Coloured glasses can also be beneficial although the optimal colours can be different from those when an overlay is used [145]. However, the efficacy of coloured overlays for Meares-Irlen syndrome (and indeed the validity of the syndrome itself) have been questioned [146]. Recent analyses have also criticised many of the studies that have been carried out with dyslexia and concluded that the use of coloured overlays and lenses is unlikely to be effective [141, 147].

Meanwhile, light has a well-known exacerbating effect on migraine headaches for about 80% of migraine sufferers, a condition known as photophobia [148]. A surprising study, however, found that even some people who were blind (from retinal damage or eye removal but with an intact optic nerve) experienced worst headaches in bright-light conditions [149]. It has now been shown that narrowband green light can actually alleviate headaches in migraine sufferers contrary to the action of other colours, and this is leading to some interesting ideas about light therapy [148].

Autism is a condition characterised by impaired social interaction, verbal and non-verbal communication, and restricted and repetitive behaviour that is usually noticed in the first two years of a child's life [150]. Some research has indicated that colour overlays could be effective in helping autistic children read more easily [151]. There has been some concern that the flicker from fluorescent lights could have an adverse effect on some repetitive

behaviours. A study of 6 autistic children showed significantly more time engaged in repetitive behaviour when illuminated by a fluorescent light than an incandescent light source [152]. However, in a study of five autistic and five mentally handicapped children no differential effect of fluorescent or incandescent light was observed on behaviour [153].

Learning, Productivity and Alertness in Indoor Spaces

The luminous environment in a space is one of the key factors affecting the occupants' work performance and mood [154]. Current concerns about sustainability may lead to a reduction in illuminance levels in office light; lighting the commercial sector account for up to 40% of energy costs in a typical UK office [155]. However, users require lighting that does not limit visual performance, does not cause visual discomfort and meets their expectations [156]. Illuminance of 500 lux is an accepted standard but it has been suggested that lower light levels may be possible without compromising the user experience [156]. The effects of illuminance (300 or 500 lux) and colour temperature (4000K or 6500K) were measured in mocked-up office rooms [157]; observers preferred the 500 lux and warmer (4000K) lighting. Some effects of spectral power distribution (rather than simply correlated colour temperature) were also observed. Although there are standards for the lux level in office environments the same is not true for correlated colour temperature (CCT) [154]. Some, although not all, studies have shown that higher CCTs appear brighter to people than lower CCTs.

High CCT lighting has shown significant improvements in self-reported measures of concentration in office workers compared with standard office lighting [158]. A study involving different types of space (such as office and living room) showed that people preferred different CCTs for different activities and suggesting changeable CCTs would be better than a fixed CCT [154]. Environmental workspace colour was varied to determine performance for low- and high-demand tasks [90]. When performing in a low-demand task performance worsened over time in the blue environment but when working in a high-demand task performance was worse in the red environment. Participants exposed to 460 nm light have been found to show decreased auditory reaction times and fewer attentional failures than when exposed to 555 nm light [158].

It has been shown 100 Hz fluorescent lighting can cause headaches and impair visual performance [159]. A study of 50 students undertaking a simple visual search task revealed better performance with light with low modulation (flicker) than with high modulation [160]. With 1200 lux lighting the speed of production of workers assembling electronic devices was higher than with 800 lux but there was no impact of light level on error rate [161]. It is not at all clear whether full-spectrum fluorescent lights (with a colour temperature of about 5000K) can give better performance than cool-white (4100K) or warm-white (3000K) fluorescent lighting [162].

Bright light can have particularly strong alerting effects at night [163] but even during the day alerting effects of bright light have been measured. For example, illumination at 1000 lux has been shown to subjective assessments of alertness and sustained attention at tasks compared with illumination at 250 lux [136].

Recently there has been much focus on the idea of dynamic lighting; lighting that varies in illuminance and colour over time [164]. Dynamically coloured lighting, for example, has been shown to decrease boredom and increase relaxation in people in a waiting environment [165]. Office workers, when assessed using a questionnaire, showed no effect of dynamic light (compared with static lighting) on alertness, headache and eyestrain, mental health, sleep quality, or subjective performance, although employees were more satisfied with the dynamic lighting [166].

A study on the effect of lighting on short-term memory and problem solving revealed better performance in warm lighting than in cool or artificial daylight lighting [91]. An earlier study found that cognitive performance might be related to the effect of the lighting on mood [167]. It has been noted that 'Color is one of the least studied aspects of the physical environment, but it nonetheless remains the topic of some of the most optimistic claims about morale and efficiency' [168, 169].

It has been shown that the colour of ambient light in a simulated car interior can have a positive effect on participants' perception of space, quality and safety [170].

The physical environment of an office space has been shown to affect creativity although with some contradictory findings with regard to colour. One study concluded that cooler colours were more conducive to creativity [171] whereas another claimed that warmer colours were more conducive [172]. In a third study no effect of colour on creativity was found [173] and the level of light has also been shown to have no effect [172] and, generally, the physical environment is thought to be less important than the social-organisational environment and the creative personality of the individual [174].

Hyperactive children are thought to be more easily under-stimulated than non-hyperactive children and it has been proposed that adding additional stimulation to a task can improve performance in case of hyperactive children [175]. The addition of colour to an otherwise black-and-white task has been effective in this regard [175]. Over the last ten years blue lights have been installed at many railway station platforms in Tokyo in an attempt to reduce suicides and were found to be effective [176-177] although recently the effectiveness has been questioned [178].

Other Medical Applications

Low-level light therapy, or photostimulation, has been suggested as an attractive alternative to enhance wound healing [179]. Use of low-level lasers was introduced in the 1970s as a treatment for wound healing [180]; low doses of laser were found to stimulate the regeneration of mechanically induced wounds and burns. Wounds generated by laser (long wavelength and infrared) surgery have been shown to heal more quickly than similar wounds generated by conventional surgery [181]. However, a study using infrared lasers on wound healing in rats found no beneficial effect [182]. Many studies are performed using red or infrared radiation but it has been shown that blue light (470 nm) can significantly influence biological systems. Blue light decreased wound size in rats and both red and blue light decreased keratin-1 mRNA [179].

Low-level laser therapy using red or infrared radiation has been used to treat various diseases involving musculoskeletal and neurologic structures [183]. For example, it has been shown to be effective to treat vestibular dysfunction and tinnitus. More recently coloured lights have been suggested as a treatment for tinnitus [184].

Summary and Future Outlook

Technology for lighting and light luminaires is rapidly changing. The consumer has mainly experienced this in terms of the range of products that are now available for home lighting, where Tungsten bulbs are being replaced in Europe by solid-state lighting, and in smart phones and tablets where a range of new technologies are producing brighter, flatter and more colourful displays. It is becoming possible and inexpensive to illuminate homes and offices so that the colour (and possibly even the spectrum) of the lighting can be changed instantly. This, however, raises interesting questions concerning which colours of lighting are most appropriate for different applications and tasks. This is leading to increased research in the effect of colour, of lighting in particular, on health, wellbeing, mood and performance. The proliferation of inexpensive coloured lighting is also leading to new uses of lighting to, for example, bring about faster healing of wounds, reduction of symptoms such as migraine and tinnitus, and alleviation of reading disorders. Whereas previously only the intensity of light used to treat seasonal affective disorder, for example, was considered to be important, now there is renewed interest in the colour or the spectrum of the lighting. Coloured lighting is being installed in various public places, with the aim of reducing certain behaviours such as suicide and anti-social activity but further research is needed to explore whether these installations are effective. It is widely believed that light and colour can affect heart rate and blood pressure, for example. However, the evidence for this is not very convincing and further work is needed to confirm these effects and the precise conditions under which they occur.

Although light clearly has great potential to positively affect health and performance, there is no doubt that it also presents a potential health threat. There is growing evidence that short-

wavelength light in particular can increase the risk of age-related macular degeneration although much of the underlying research that has been carried out has been done on animals. There is still no conclusive proof that bright short-wavelength light increases risks in humans. It remains to be seen whether increased use of emissive displays, changing working habits, and the replacement of warm interior lighting in the home with light of a much higher correlated colour temperature present real risks in terms of retinal damage and age-related macular degeneration. 'Blue light at night' is another potential health risk. Excess light at night is probably partly responsible for poor sleeping experiences and this also has some associated health risks around diabetes and heart disease. Insufficient light in the day can lead to depression and myopia. A sensible way forward, however, is to have lots of high-CCT light in the day and not very much at night (the scenario in which we evolved for millions of years). There is also a substantial potential for dynamic lighting to be used to better illuminate our homes, workplaces and cities. It is clear that the spectral power of light (rather than its CCT) may be required in many cases in order to properly assess risk or benefit. The biggest risk of light today, however, probably remains skin cancer.

Colour and light undoubtedly affect mood and our perception of our environment. However, research to explore the effects of colour and light on learning, autism, reading, and creativity still has a long way to go before definitive conclusions can be made.

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