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MINI REVIEW

The dark side of light at night: physiological, epidemiological, and ecological consequences

Abstract: Organisms must adapt to the temporal characteristics of their surroundings to successfully survive and reproduce. Variation in the daily light cycle, for example, acts through endocrine and neurobiological mechanisms to control several downstream physiological and behavioral processes. Interruptions in normal circadian light cycles and the resulting disruption of normal melatonin rhythms cause widespread disruptive effects involving multiple body systems, the results of which can have serious medical consequences for individuals, as well as large-scale ecological implications for populations. With the invention of electrical lights about a century ago, the temporal organization of the environment has been drastically altered for many species, including humans. In addition to the incidental exposure to light at night through light pollution, humans also engage in increasing amounts of shift-work, resulting in repeated and often long-term circadian disruption. The increasing prevalence of exposure to light at night has significant social, ecological, behavioral, and health consequences that are only now becoming apparent. This review addresses the complicated web of potential behavioral and physiological consequences resulting from exposure to light at night, as well as the large-scale medical and ecological implications that may result.

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Introduction

Successful organisms must adapt to temporal, as well as spatial niches. Endogenous biological clocks allow individuals to anticipate and adapt to the daily light-dark cycles in their environments to optimally time metabolism, physiology, and behavior each day. Rodents in nontropical environments, for example, alter reproductive, metabolic [1], and immunological activities [2] based on changes in day length throughout the seasons. The timing of avian reproduction and molt also often depends upon seasonal changes in day length [3], and many species, including some birds [4,5], rodents [6], bats [7], and marine animals [8], adjust foraging activities according to changes in the lunar cycle. Aside from seasonal adjustments, there is marked circadian variation in physiological functions. In many species, including some birds, rodents, fish, and humans, for example, circulating concentrations of sex steroids [9–11] and glucocorticoids [12] vary with the light/dark cycle throughout the day, causing corresponding changes in reproductive activities [13] and metabolic functions [14].

Responses to natural light cycles result in an adaptive temporal organization in humans and other animals. With the invention and use of electrical lights, beginning about a century ago, this temporal organization has been dramatically altered. Light at night has significant social, ecological, behavioral, and health consequences that are only now becoming apparent. The extensive control that light-driven mediators exert upon multiple body systems, for example, creates numerous targets on which light-induced disruptions can act, resulting in a wide range of physiological changes and potentially serious medical implications. In a broader context, underpinning physiological mechanisms regulate a variety of behaviors, ranging from reproduction to foraging, creating expansive targets for light disruption. Assuming that adaptive processes have optimized the physiological and behavioral regulation of animals according to changing day lengths and circadian cycles, artificial changes in light cycles could have drastic fitness effects. This review summarizes the medical and ecological implications of exposure to artificial light at night, and related disturbances in normal seasonal and circadian physiological and behavioral functions.

Sources of light at night

Light pollution by urban development

Urban development has brought the need for artificial lighting of roadways, shopping centers, stadiums, and homes. Some of this light strays and scatters in the atmosphere, bringing about a brightening of the natural sky beyond background levels, called urban sky glow [15,16]. Light pollution has demonstrated effects on daily

human life. In 2001, the percentage of the world's population living under sky brightness higher than baseline levels was 62%, with the percentages of US and European populations exposed to brighter than normal skies lying at 99% [16]. In addition, >80% of the US population and 2/3 of the population in the European Union regularly experience sky brightness greater than nights with a full moon. In these cases, true night darkness is never experienced because the brightness is slightly higher than the typical zenith brightness at nautical twilight [16]. Since the 1960s, artificial lighting has gradually changed from an incandescent-bulb form, which consists of mainly low-level yellow wavelengths, to a high-intensity discharge (HID) form that contains blue wavelengths (reviewed in [17]). Retinal ganglion cells responsible for detecting light and suppressing melatonin production in humans are most sensitive to blue/violet light (~459 nm) [18]. In addition, studies on the action spectrum for human melatonin regulation indicate that exposure to incandescent lighting for $<1\,$h can result in a 50% decrease in circulating melatonin levels, and exposure to even very low levels of blue spectrum light comparable in brightness to moonlight resulted in melatonin suppression in humans as well (reviewed in [17]). Thus, increasing levels of sky glow and exposure to street lighting can disrupt the 'natural' world to which the human body is currently adapted.

While humans live much of their lives based on artificially manipulated light cycles governed by electric lighting, wild species are entirely dependent upon and responsive to changes in natural day length. Thus, photic disturbances that alter the natural light cycle may have elevated physiological and behavioral effects in these species compared with humans. Many 'wild' or national parks are surrounded by or in close proximity to urban centers, causing increased incidence of sky glow over those areas [15], thus exposing many wild species to an artificial and potentially disruptive light cycle.

Shift work

In addition to incidental light exposure resulting from night lighting, current society is experiencing an abolishment of 9–5 workdays in exchange for greater numbers of night shifts and resulting increases in productivity and profit. For example, North American fast-food restaurants began gleaning profits during the late night and early morning hours as early as the mid-1990s (MSNBC.com, 2004). In addition, in a survey conducted from 1985 to 2004, approximately 15% of surveyed American full-time wage and salary workers worked a shift other than a daytime schedule; over half of these workers reported that such hours resulted from 'the nature of the job' and not personal preference (US Dept. of Labor, 2004). Such trends not only exist in the USA, but also in Canada where approximately 30% of employed individuals work alternative shifts [19]; overall, in any urban society, an estimated 20% of people work alternative shifts [20]. Shift-workers live much of their lives out-of-phase with 'normal' local time, but often cannot completely adjust their circadian rhythms due to the changing schedules of the shift-work, and the necessary readjustment to rest days [20]. Thus, shift-workers are experiencing intentional exposures to light at night that could disrupt normal circadian physiological and behavioral rhythms.

Physiological and medical implications

The circadian pacemaker is responsible for organizing the timing of the entire body, spanning multiple body systems [21–24]. Light is detected by photoreceptive ganglion cells (pRGCs) in the eye. A cluster of pRGCs form the retinohypothalamic tract that projects to and entrains a group of neurons that make up the circadian oscillators in the suprachiasmatic nuclei (SCN) [25], which control melatonin synthesis in the pineal gland. Melatonin is an indole-amine that is found throughout the animal kingdom and orchestrates changes in many physiological functions in response to variation in day length (reviewed in [26]), and the nightly duration of melatonin is the critical parameter responsible for transducing the effects of light on both the neuroendocrine axis and directly on individual body systems [27]. Exposure to extended periods of light alters melatonin in many species, including humans [28–31]. Thus, exposure to light at night could result in a variety of physiological effects, potentially mediated through varying levels of melatonin (Fig. 1). In addition, direct sympathetic control of physiological processes after variation in lighting conditions has been documented independently of melatonin synthesis [1]. Consequently, exposure to extended periods of light could alter physiological state through a variety of mechanisms.

Disruptions of normal circadian timing can evoke a multitude of downstream effects, reorganizing the entire physiological state. Constant lighting conditions alter the

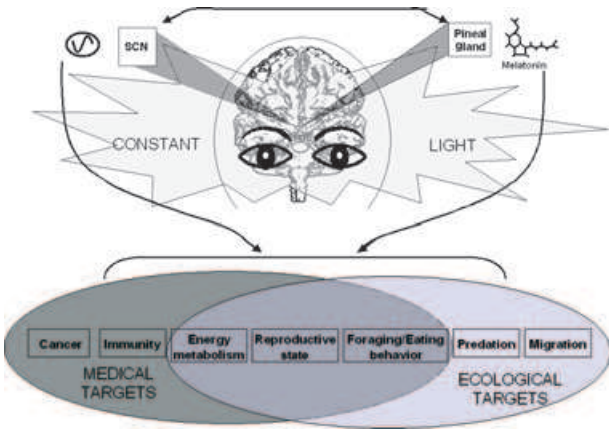

Fig. 1. Exposure to night-time lighting through urban sky glow and/or night shift work could mimic the documented physiological and behavioral effects associated with exposure to constant levels of light. These effects are complex and multi-tiered, and could have large-scale medical and/or ecological implications. Light detected by the retinal ganglial cells (RGCs) programs the suprachiasmatic nuclei (SCN), or the circadian pacemaker. The SCN exerts direct effects on several body systems and stimulates rhythmic melatonin secretion from the pineal gland. Melatonin acts as a transducer of light:dark information into additional physiological signals that results in downstream effects on many body systems. (arrows are not meant to represent exact anatomical locations).

rhythmicity of several hormones including prolactin [32], glucocorticoids [33,34], adrenocorticotropic hormone, corticotrophin releasing factor [35], serotonin [36], and melatonin [37]. Human exposure to a low-level incandescent bulb at night requires only 39 min to suppress melatonin levels to 50% [38]. Such changes in melatonin production and release regulates metabolism, immune function, and endocrine balances via the reproductive, adrenal, and thyroid hormone axes [27]. The ensuing effects of disrupted melatonin rhythms by chronic exposure to light at night would be countless. In addition, the effects resulting from downstream consequences, such as sleeplessness, make the web of physiological changes resulting from constant light even wider. In the interest of space, the medical implications associated with sleep deprivation will not be considered in depth here. Recent work has largely focused on the potential link between exposure to artificial light at night and the prevalence of several cancers (see below). Such links, however, would likely result from a combination of upstream physiological effects originally triggered by the alteration of the circadian system, many of which could have drastic medical implications in addition to cancer. For example, melatonin and its metabolites have the ability to protect against oxidative stress and diseases resulting from oxidative attack (see below). Depression of melatonin could thus magnify the amount and results of oxidative damage. There is a need for a full understanding of the physiological and epidemiological impacts caused by increasing exposure to light at night through light pollution and shift work.

Metabolic disruption

Efficient energy metabolism is crucial to overall physiological well-being. Interruptions or difficulties with the efficiency of metabolic processes can result in a variety of disorders, including obesity, type II diabetes, and heart disease. There is an abundance of evidence illustrating an effect of exposure to extended levels of artificial light both directly on metabolic processes, as well as on several of these end-points.

Long-term exposure of rats to constant light had strong regulatory effects on metabolism, specifically on carbohydrate metabolism in the liver [39]. Experiments on broiler chickens demonstrated that constant light shifts metabolic efficiency; female broiler chickens reared in a constant light environment gained a significantly higher percentage of fat compared with controls reared on a 12 L:12 D light cycle. Male broiler chickens also gained significantly more weight when exposed to constant light, but the mechanism behind this effect differed (i.e. food intake was higher in males reared in constant light) [40]. Constant-light induced interruption in the nightly secretion of melatonin can also exert metabolic effects. Melatonin appears to affect body mass regulation, gut efficiency, metabolic rate, and non-shivering thermogenesis in some mammalian species (reviewed in [26]), and also improves ATP synthesis in the heart [41]. Thus, the basic processes associated with acquisition and utilization of energy are functionally altered after exposure to extended periods of artificial lighting.

Several studies suggest that humans are experiencing similar effects in response to artificial light exposure at night. For example, detrimental effects of shift work have been observed in carbohydrate and lipid metabolism, insulin resistance, hypertension, coronary heart disease, and myocardial infarction (reviewed in [42]). Such influences could result from either direct physiological effects of light exposure or indirect effects associated with a lack of sleep [42]. Sleep deprivation significantly alters endocrine and metabolic parameters associated with diabetes, obesity, and a cascade of other disorders [43]. On the other hand, melatonin levels, which reflect changes in light environment more directly, have been associated with coronary heart disease. For example, in a correlative study, patients with coronary heart disease had significantly lower melatonin concentrations at night compared with patients without heart disease [44]. Melatonin reduces the activity of the sympathetic nervous system and significantly reduces norepinephrine turnover in the heart, a potentially beneficial effect because norepinephrine and epinephrine accelerate the uptake of LDL cholesterol [45]. Because exposure to extended periods of low-level artificial night-time lighting decrease melatonin production in rodents [28,45] and humans (reviewed in [17]), the potential for a direct link between exposure to night-time light and metabolic disorders, such as heart disease, become clear. It remains to be determined that the extent to which metabolic disorders reflect direct effects of light on circadian organizations or down-stream processes such as sleep disruption.

Oxidative stress

Light exposure can also have indirect adverse effects through the promotion of oxidative stress, which can lead to a variety of other disorders, including damage to immune cells and other tissues in the body, elevated incidence of cancer, and an increase in the rate of physiological aging [46]. Exposure of living organisms to light and oxygen results in the production of toxic molecules, reactive oxygen species, and photo-oxidants (reviewed in [47]). For example, rats maintained in constant light significantly increased lipid peroxidation in the liver, kidney, and brain [28]. Similarly, rats exposed to constant light significantly elevate levels of hepatic oxidative stress [48]. Oxidative stress is combated through numerous physiological mechanisms responsible for maintaining an oxidant:antioxidant balance within the body. Melatonin is a well-known antioxidant, playing a significant role in antioxidant defense and regulating antioxidant enzyme activity and production (reviewed in [49]). In humans, melatonin levels correlate with total antioxidant capacity of the blood [50]. Constant light reduces both melatonin levels and pineal weights to a minimum [28] and the pro-oxidative effects of constant light were preventable through simultaneous administration of melatonin [28]. Activity of glutathione peroxidase, an important antioxidant enzyme, decreased in rats maintained in constant light [28]. Similarly, constant light exposure reduces glutathione levels [51], suggesting a decrease in glutathione production as well. It is likely that suppression of melatonin in response to constant light exposure may at least partially mediate the regulation of glutathione peroxidase activity, as previous studies have shown that melatonin stimulates glutathione

synthesis [52] and melatonin deficiency leads to decreased tissue glutathione peroxidase activity (discussed in [28]). Melatonin is unique in that the free radical scavenging capability extends to its secondary, tertiary, and quaternary metabolites, making it a highly effective antioxidant even at low concentrations (see [47] for review). Thus decreased levels and durations of melatonin production resulting from exposure to constant lighting conditions may result in decrease in the level and duration of this potentially important antioxidant. Alternatively, influences of changing the light environment on oxidative stress could result from downstream consequences of resulting sleep deprivation as has been documented in the brains of rats [53]. Considered together, these documented reductions in melatonin concentrations in humans exposed to night-time light suggest an elevated risk of oxidative stress and many related disorders after exposure to light pollution, shift work, or both.

Immunological modulation

Exposure of an individual to chronic artificial night-time lighting could alter immune function, through some combination of oxidative, neural, or endocrine pathways. Numerous examples across taxa are available. For example, housing Japanese quail (*Coturnix coturnix japonica*) in constant lighting conditions significantly suppressed both cell-mediated immune responses to a challenge with phytohemagglutinin (PHA) and humoral responses to challenges with Chukar red blood cells (RBCs) [54]. Similarly, cockerels maintained in constant lighting conditions produced significantly fewer antibodies to a challenge with sheep RBCs and displayed significantly reduced delayed type hypersensitivity responses compared with controls maintained in 12 L:12 D lighting conditions [55]. In a mammalian model system, nocturnal light exposure suppressed the normal increase in cytotoxic activities of natural killer cells [56].

Because exposure to light at night is accompanied by a significant decrease in melatonin levels (see above), it is relevant to briefly discuss the potent effects that melatonin has on the immune system. The injection of Syrian hamsters with melatonin, or maintenance of hamsters in short photoperiods which increase melatonin levels resulted in increased splenic masses, total splenic lymphocyte counts, and macrophage numbers [57]. A number of studies have confirmed the existence of melatonin receptors in lymphatic tissue and on circulating cells of the immune system (reviewed in [26]). Although prevalence of splenic melatonin receptors typically fluctuate such that receptor numbers are low at night when melatonin levels are high, levels of binding sites during light at night remain high [58]. Melatonin has been reported to counteract drug or hormone-based immunosuppression and appears to have generally immunostimulatory properties (reviewed in [26]). Suppression of melatonin by exposure to light pollution or during shift work could suppress such immunostimulatory properties. On the other hand, constant light generally inhibits T-cell autoimmunity by eliminating melatonin [26], a potentially beneficial effect. Carrillo-Vico et al. provide an excellent review of the effects of melatonin on the immune system [59]. Based on these documented effects, the potential exists for artificial night-time light to have potent and multi-pathway modulatory effects on the immune system. Similar effects could result from decreases in sleep efficiency associated with exposure to constant levels of light. For example, in a study of humans, 40 h of wakefulness resulted in significant changes in several immune parameters, including a decrease in natural killer cell activity [60]. Sleep deprivation also activates the HPA axis in rats and alters subsequent responses to stress [61], which could exert indirect effects on the immune system as well. Thus, through either direct endocrine effects or indirect sleep-related effects, exposure to light at night has the potential to significantly modulate immune function, leading to large-scale medical implications.

Cancer

Resistance to cancer is often accomplished through endocrine, antioxidant, and immunological processes. It is now apparent that all of these processes can be altered by exposure to light at night; evidence is mounting that forms links between extended exposure to light and the incidence of several cancers in both humans and animals. For example, the risk of developing breast cancer is up to five times higher in industrialized nations than in underdeveloped countries [62]. Current evidence suggests that high levels of artificial light at night in industrialized societies may play a role in cancer risk. Multiple studies have documented a link between night shift work and an increased incidence of breast cancer (reviewed in [63]). In a nationwide study of 7035 Danish women with confirmed primary breast cancer, at least half a year of predominantly work during the night increased the risk of breast cancer 1.5 fold [64]. Other studies of women involved in various types of work during the night have consistently demonstrated an up to threefold increase in the relative risk of breast cancer ([64], also see [65] for review). Although night shift work increased the incidence of breast cancer, an increased risk was also documented in individuals who reported not sleeping during the time of night when melatonin is typically elevated [66]. Importantly, there was an indication of increased risk in patients with the brightest bedrooms [66]. Although breast cancer is the most abundantly studied cancer type in relation to light at night and shift work, recent studies have begun examining links with other cancer types. For instance, in a study of 602 colorectal cancer cases among 78,586 women, it was determined that a rotating night shift at least three nights per month over at least 15 yr increases the risk of colorectal cancer [67]. Considered together, abundant evidence suggests that circadian disruption, and/or the changes in melatonin and other physiological systems may increase the risk of cancers.

Specific evidence of the role of light in tumor development was demonstrated in deer mice (*Peromyscus maniculatus*); mice maintained in long day lengths (16 L:8 D) were significantly more likely to develop tumors induced by 9,10-dimethyl-1,2,benzanthracene (DMBA) compared with animals maintained in short day lengths (8 L:16 D) [68]. Indeed, 90% of animals in long day lengths developed tumors, whereas animals maintained in short day lengths

developed none. More recent studies have demonstrated that exposure to extended dim light can have similar effects on tumor incidence and growth. Exposure to constant dim light (0.21 lux) significantly increased the growth of MCF-7-induced tumors and significantly increased the total tumor fatty acid uptake, linoleic acid uptake, and 13-hydroxyoctadecadienoic acid (13-HODE) production (reviewed in [69]). Additionally, female rats with small DMBA-induced tumors were maintained in one of the four treatment groups, including a normal light cycle (12 L:12 D), a constant bright light cycle (24 h at 300 lux), a normal light cycle with a flash of bright light halfway through the dark period, and a normal cycle with low level incandescent lighting throughout the dark period [70]. Animals maintained in the normal light cycle (12 L:12 D) had significantly lower rates of tumor growth than all other treatments, and the animals experiencing dim light at night had the lowest survival probability. In summary, extended periods of exposure to even dim levels of light impair suppression of tumor development.

Both experimental and clinical reports suggest a link between cancer development and pineal function (reviewed in [26]). Under a majority of in vitro conditions, physiological levels of melatonin decrease the rate of cell proliferation, whereas elevated concentrations tend to be either cytostatic or cytotoxic (reviewed in [69]). Melatonin may shift the cell balance from proliferation to differentiation, and thus can prevent the proliferation of tumor cells. In addition, melatonin may promote apoptosis of cancer cells (reviewed in [69]). Pinealectomy accelerates the growth of transplanted melanoma in hamsters [71] and of transplanted Yoshida sarcoma in rats [72]. In addition, DMBA-induced mammary tumors grew more slowly in rats treated with melatonin when compared with control rats that did not receive melatonin ([73], reviewed in [74]). In a particular elegant study, rats were implanted with either rat hepatomas or human breast cancer xenografts [62]. Resulting tumors were subsequently perfused in situ with human blood collected from subjects during the daytime, during the night, or following exposure to 580 $\mu W/cm^2$ of white fluorescent light at night. In addition, some of the blood collected from individuals exposed to night-time light was also supplemented with a synthetic form of melatonin. Proliferative activity, linoleic acid production, 13-HODE production, and tumor cAMP levels significantly decreased when tumors were exposed to blood taken from individuals during the night-time. This suppressive effect disappeared when tumors were exposed to blood from individuals who experienced night-time light, leaving proliferation levels similar to those perfused in blood from daytime individuals. Interestingly, when melatonin was added to blood from light-exposed individuals, tumor proliferation and activity was again suppressed [62]. These data suggest that melatonin exerts a direct effect on tumor growth and proliferation.

Constant light may act on cancer through direct actions of depressed melatonin levels or through secondary endocrine modulation associated with either light exposure resulting from light exposure and/or sleep disruption [63,65]. 'The melatonin hypothesis' suggests that reduced pineal melatonin secretion might increase the risk of breast cancer through an interaction with high levels of estrogen, a known promoter of breast tissue proliferation [75]. Melatonin is a known suppressor of estrogen secretion in several species of mammals [76]. Melatonin completely blocks estradiol-induced stimulation of breast cancer cell proliferation, and melatonin loses its antiproliferative effects unless cells are co-cultured with estradiol or prolactin [77]. As mentioned, melatonin acts as a potent antioxidant, and thus may normally protect against estradiol-induced oxidative damage that could result in cancer (reviewed in [78]). Alternatively, melatonin may prevent the estradiol-induced suppression of the cell-mediated immune response, providing immunological protection against cancer development (reviewed in [78]). Estradiol is also responsible for upregulating telomerase activity, and melatonin may inhibit these effects. Thus, suppression of melatonin after exposure to constant light would inhibit these anti-cancer effects. Despite this evidence, rats exposed to constant light did not increase serum estradiol concentrations [62,68]. Furthermore, ovariectomy and estrogen treatment did not affect tumor formation [68]. Thus, although the 'melatonin hypothesis' seems plausible, current evidence suggests that light exposure likely acts on tumor formation and growth through one or more alternative mechanisms.

Ecological implications

Physiological responses to artificial light exposure result not only in the medical conditions listed above, but also in large-scale ecological changes. Natural departures from the rhythmic light:dark cycle, such as changes in the lunar cycle and white nights in the artic region of the world, evoke a multitude of physiological and behavioral changes within animals experiencing them [79] (and see below). Because sky glow resulting from artificial lighting in urban environments can reach levels that exceed those seen in natural twilight [16], similar physiological and behavioral phenomena may result, altering reproductive activities, predator/prey interactions, and even orientation capabilities. Such alterations in natural activities can result in large-scale ecological changes, and alterations in the survival of key species in the environment (See [80] for an excellent additional detailed review addressing ecological light pollution).

Reproduction

It has been well-established that the timing of breeding in wild animals could be altered by artificial lighting. For example, it has been known for centuries that domestic hens (*Gallus domesticus*) could be stimulated to lay more eggs during the winter by putting lights in the coops at night [81]. In one of the first studies of the effects of photoperiod on vertebrate biology, Rowan (1925) [82] exposed juncos (*Junco hyemalis*), maintained in outdoor aviaries in Edmonton, Alberta, to several minutes of electric illumination after the onset of dark each day (lights were illuminated at sunset) during the winter. Under these artificial lighting conditions, these birds came into reproductive condition despite the harsh Canadian winter temperatures. Thus, artificial lights were sufficient to adjust

the reproductive phenotype of these birds to mimic summer-like conditions. Similarly, the initial demonstration that photoperiod regulates mammalian reproduction was reported for European field voles (*Microtus agrestis*) that received artificial illumination after the onset of dark [83]. Again, artificial illumination effectively mimicked natural light sources.

Given the level of control that variation in light cycles can exert on reproductive physiology and behavior, exposure to lighting durations beyond normal limits can impose disruptive effects on these processes. Melatonin, for example, has well-documented effects on reproductive behavior and physiology in many species [76], and exposure to extended periods of light depress production of pineal melatonin [28–31]. Such effects may mediate the documented changes in the reproductive systems of animals in response to extended exposure to light. For example, persistent exposure to constant dim light suspends estrous cycles in rats and induces persistent estrus [84]. Such disruption reduces fertility [80] by inhibiting periovulatory gonadotropin surges [85,86] and elevating plasma prolactin and estrogen concentrations [32,84,87]. Similarly, exposure of male South Indian gerbils (*Tatera indica cuvieri*) to constant light diminished reproductive efficiency, decreasing reproductive organ masses, epididymal sperm counts, and the proportion of ejaculating males [88]. Maintenance in constant light is a well-documented way of interrupting incubation in turkey hens, and results in significantly elevated prolactin concentrations in circulation [89] and trout exposed to either constant or 18 h of light advanced spawning up to 2 months compared with control fish exposed to ambient light [90]. Such changes in the timing of reproduction could disrupt synchrony of the breeding cycle in relation to changing environmental variables, such as temperature. In cases where sky brightness never gets below the level of a typical nautical twilight [16], reproductive disruption is a clear possibility for a number of species.

Evidence that light pollution and exposure to artificial lighting disrupts reproductive activities in the wild has been demonstrated in studies examining behaviors and activities associated with reproduction in a wide range of species. For example, artificial illumination influenced territorial singing behavior in mockingbirds (*Mimus polyglottos*); after mating, male mockingbirds only sang in artificially lighted areas, or during the full moon ([91]; reviewed in [80]). In frogs, male mating calls may be disrupted by artificial lighting, and female frogs *Physalaemus pustulosus*, are less selective about mate choice and mate earlier under increased lighting levels. It has been suggested that advancing reproduction is a method of avoiding predation due to extended exposure under well-lit conditions (reviewed in [80]). Black-tailed godwits (*Limosa l. limosa*) based their choices of nesting sites according to roadway lighting, choosing to nest approximately 300 m away from artificial roadway lighting (reviewed in [80]). Such disruptive effects of artificial lighting even extend into invertebrate animal classes. Female glowworms, for example, attract males with visual flashes that are less visible in lighted environments (reviewed in [80]). Interruptions in such critical reproductive behaviors mediated by exposure to artificial lighting could exert significant fitness consequences for a wide variety of animal species.

Foraging and predation

Predator-prey interactions are important determinants of many decisions made by animals, ranging from foraging behavior to mate choice (reviewed in [92,93]). It is well established that dynamics of predator-prey interactions change as a function of ambient light levels. For example, foraging behavior decreases during high lunar illumination in desert and temperate rodents [94,95], fruit eating bats (*Artibeus jamaicensus*) [96], small seabirds [93], and even in nonvisual predators, such as scorpions (*Buthus occitanus*) [97]. Light drives a number of animals to make activity decisions either directly by changing the risk of being seen by a predator (Predation Risk Hypothesis, reviewed in [93]) or indirectly by altering prey availability and thus changing the payoff of foraging during times of high illumination (Foraging Efficiency Hypothesis [98]). These ideas are not mutually exclusive and in some cases, illumination has both direct and indirect effects. For example, foraging efficiency of short-eared owls (*Asio flammeus*) increases in bright moonlight and, at the same time, the activity levels and foraging behavior of their prey, deer mice (*P. maniculatus*) decreases to avoid the increased risk of being eaten in a highly illuminated environment [94]. Similarly, variation in light levels produces a significant shift in the capture rates of prey by the lined seahorse (*Hippocampus erectus Perry*) [99]. Thus, changes in illumination levels affect not only the behaviors of predators, but also the behaviors of their prey as well as any other species directly linked to their prey. Such a phenomenon could result in large-scale ecosystem changes (see [80] for review).

In some parts of the world, sky brightness resulting from urban sky glow is even greater than nights with a full moon [16]. Thus, if natural lunar cycles exert such dramatic effects on predator-prey interactions, then artificial light resulting from sky glow could have equal, if not more dramatic, changes on ecological dynamics. Indeed, artificial lighting exerts strong effects on foraging behavior and predation. For example, artificial illumination increased the predatory risk for and reduced foraging behavior in three rodent species, including the Arizona pocket mouse (*Perognathus amplus*), Bailey's pocket mouse (*Perognathus baileyi*), and Merriam's kangaroo rat (*Dipodomys merriami*) [100]. Similar results were obtained in additional species of desert rodents [6] and artificial illumination also affects the foraging behavior of petrels [98].

In some cases, high levels of illumination are purposely used by animals to aid foraging abilities. Foraging northern bats (*Eptesicus nilssoni*) in Sweden are attracted to illuminated roadways in the Spring [101]. The numbers of insects congregating and bats foraging around three types of street lamps was monitored in one study [102]: 125 W Hg lamps which give off a bluish-white light, 100 W high pressure Na lamps which give off a light orange light, and 100 W low pressure Na lamps which give off a deep orange light. Insects were most abundant around the bluish-white light, and also significantly abundant around the light orange light, whereas insect numbers around the deep orange light

were similar to lamps that were turned off. Additionally, several bat species foraged more in the areas illuminated by the bluish-white and light orange lights [103]. Thus, bright streetlamps emitting light in the blue wavelengths draws many insects towards a high risk of predation, and abundance of these lighting sources could result in a change in the survival and propagation of many insect species. The mechanistic basis for such changes in foraging behaviors remains elusive for most species. In some species of birds, constant lighting may alter foraging activities through the alteration of natural melatonin rhythms [104] and melatonin has also been shown to regulate food intake in mammals (reviewed in [26]). Thus changes in melatonin levels and/or other physiological signals resulting from constant light exposure may regulate foraging behavior in other species as well. The implications for large-scale ecological impacts resulting from artificial illumination in this manner are clear.

Migration and orientation

Migration is a critical event in the lives of many animals and is often necessary for successful reproduction and survival. Changes in ambient illumination drive migration patterns in a variety of species [82,103,105–107]. Silver eels (*Anguilla anguilla* L.), for example, exhibit 'light shyness' because they cease 'running' (migrating) when lunar illumination levels are high [108]. In salmonid fishes, exposure to the new moon triggers a thyroxine surge that is thought to trigger the onset of migration towards the sea [109]. Many aquatic invertebrates exhibit 'diel vertical migration', movement up and down the water column, according to changes in lunar illumination; some species of zooplankton and shrimp avoid surface water layers in response to light dimmer than that of a half moon (reviewed in [80]).

Exposure to sky glow and artificial lighting that is currently common can have severe effects on the migratory patterns of animals. Changes in migration patterns in response to artificial light exposure were documented long ago in crows (*Corvus brachyrhynchos*) [82] and in some cases, migrating birds become attracted to and disoriented by artificial night lighting (reviewed in [80]). Silver eel (*Anguilla anguilla* L.) exposed to underwater electric lighting ceased migrating [107] and disruption of the circadian clock of monarch butterflies (*Danaus plexippus*) interfered with their orientation direction during migration [103]. Exposure of the zooplankton *Daphnia* to urban light pollution in the wild decreased the magnitude of migratory movements and the number of migrating individuals [106]. One markedly disruptive form of light pollution interference is the effect of artificial light on hatchling sea turtles. After hatching, sea turtles orient themselves towards the sea using a visual cue – they move away from the shadowy backdrop of the low sand dunes. Artificial lighting associated with beachfront urbanization removes that visual cue and disorients the young sea turtles [110].

The mechanistic basis behind such changes in migratory patterns and behaviors remains to be elucidated; however, studies in birds have shown that melatonin plays a crucial role in the timing and orientation aspects of avian migration [111,112]. Thus changes in migratory behavior may result from alterations in melatonin levels and/or other circadian and seasonally based physiological signals. Changes in the timing and/or efficiency of migration and general orientation can be detrimental in terms of both survival and reproduction. Even low levels of artificial lighting effectively mimic the natural influences of the lunar cycle. Urban sky glow causes sky brightening long distances from the original lighting source, potentially affecting migrating individuals kilometers away [15]. Such large-scale changes could have drastic ecological impacts.

Future directions

Irregular light/dark patterns are now being considered as endocrine disruptors [45]. Indeed, the material summarized in this review illustrates a multitude of physiological effects, most of which occur through endocrine pathways after exposure to extended periods of light. Should exposure to light be regulated as endocrine disrupting compounds in the environment? Proposals have been put forth to decrease levels of urban sky glow through light shields, reduction in the number of lights, as well as through an adjustment of the color spectrum produced by external lighting towards low-level red lighting and away from the highly disruptive high-energy blue lighting. It is clear that increasing levels of urban sky glow can have serious medical and ecological repercussions (Fig. 1). Additionally, elevated numbers of night shifts worked could result in large-scale incidences of metabolic disorders, immunosuppression, oxidative stress, and cancer. Future work should examine both the epidemiological end-points associated with exposure to light pollution and circadian disruption, as well as the endocrine mediators that may be involved. A thorough understanding of the mechanisms by which exposure to unnatural patterns of light may alter specific components of physiology and behavior could be useful towards the implementation of plans to combat large-scale medical and ecological disruptions associated with disturbances in the natural light cycle.

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