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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 retino-hypothalamic 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

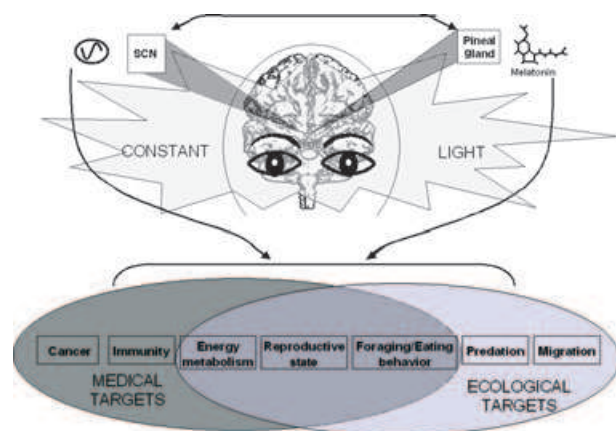


Fig. 1. Exposure to night-time lighting through urban sky glow and/or night shift work could mimic the documented physiological and behavioral effects associated with exposure to constant levels of light. These effects are complex and multi-tiered, and could have large-scale medical and/or ecological implications. Light detected by the retinal ganglionic 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).

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

31 **Metabolic disruption**

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

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

60 Several studies suggest that humans are experiencing
 61 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 influ-
 ences 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 nor-
 epinephrine 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 disor-
 ders, 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 simulta-
 neous administration of melatonin [28]. Activity of gluta-
 thione peroxidase, an important antioxidant enzyme,
 decreased in rats maintained in constant light [28]. Simi-
 larly, 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

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

21 Immunological modulation

22 Exposure of an individual to chronic artificial night-time
23 lighting could alter immune function, through some com-
24 bination of oxidative, neural, or endocrine pathways.
25 Numerous examples across taxa are available. For example,
26 housing Japanese quail (*Coturnix coturnix japonica*) in
27 constant lighting conditions significantly suppressed both
28 cell-mediated immune responses to a challenge with phy-
29 tohemagglutinin (PHA) and humoral responses to chal-
30 lenges with Chukar red blood cells (RBCs) [54]. Similarly,
31 cockerels maintained in constant lighting conditions pro-
32 duced significantly fewer antibodies to a challenge with
33 sheep RBCs and displayed significantly reduced delayed
34 type hypersensitivity responses compared with controls
35 maintained in 12 L:12 D lighting conditions [55]. In a
36 mammalian model system, nocturnal light exposure sup-
37 pressed the normal increase in cytotoxic activities of natural
38 killer cells [56].

39 Because exposure to light at night is accompanied by a
40 significant decrease in melatonin levels (see above), it is
41 relevant to briefly discuss the potent effects that melatonin
42 has on the immune system. The injection of Syrian
43 hamsters with melatonin, or maintenance of hamsters in
44 short photoperiods which increase melatonin levels resulted
45 in increased splenic masses, total splenic lymphocyte
46 counts, and macrophage numbers [57]. A number of studies
47 have confirmed the existence of melatonin receptors in
48 lymphatic tissue and on circulating cells of the immune
49 system (reviewed in [26]). Although prevalence of splenic
50 melatonin receptors typically fluctuate such that receptor
51 numbers are low at night when melatonin levels are high,
52 levels of binding sites during light at night remain high [58].
53 Melatonin has been reported to counteract drug or
54 hormone-based immunosuppression and appears to have
55 generally immunostimulatory properties (reviewed in [26]).
56 Suppression of melatonin by exposure to light pollution or
57 during shift work could suppress such immunostimulatory
58 properties. On the other hand, constant light generally
59 inhibits T-cell autoimmunity by eliminating melatonin [26],
60 a potentially beneficial effect. Carrillo-Vico et al. provide
61 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 endo-
crine, 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 underdevel-
oped 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 dis-
ruption, 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 develop-
ment was demonstrated in deer mice (*Peromyscus manicu-
latus*); 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 ani-
mals 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 $580 \mu\text{W}/\text{cm}^2$ 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 arctic 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

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

8 Given the level of control that variation in light cycles
 9 can exert on reproductive physiology and behavior,
 10 exposure to lighting durations beyond normal limits can
 11 impose disruptive effects on these processes. Melatonin,
 12 for example, has well-documented effects on reproductive
 13 behavior and physiology in many species [76], and
 14 exposure to extended periods of light depress production
 15 of pineal melatonin [28–31]. Such effects may mediate the
 16 documented changes in the reproductive systems of
 17 animals in response to extended exposure to light. For
 18 example, persistent exposure to constant dim light sus-
 19 pends estrous cycles in rats and induces persistent estrus
 20 [84]. Such disruption reduces fertility [80] by inhibiting
 21 periovulatory gonadotropin surges [85,86] and elevating
 22 plasma prolactin and estrogen concentrations [32,84,87].
 23 Similarly, exposure of male South Indian gerbils (*Tatera*
 24 *indica cuvieri*) to constant light diminished reproductive
 25 efficiency, decreasing reproductive organ masses, epididy-
 26 mal sperm counts, and the proportion of ejaculating males
 27 [88]. Maintenance in constant light is a well-documented
 28 way of interrupting incubation in turkey hens, and results
 29 in significantly elevated prolactin concentrations in circula-
 30 tion [89] and trout exposed to either constant or 18 h of
 31 light advanced spawning up to 2 months compared with
 32 control fish exposed to ambient light [90]. Such changes in
 33 the timing of reproduction could disrupt synchrony of the
 34 breeding cycle in relation to changing environmental
 35 variables, such as temperature. In cases where sky
 36 brightness never gets below the level of a typical nautical
 37 twilight [16], reproductive disruption is a clear possibility
 38 for a number of species.

39 Evidence that light pollution and exposure to artificial
 40 lighting disrupts reproductive activities in the wild has been
 41 demonstrated in studies examining behaviors and activities
 42 associated with reproduction in a wide range of species. For
 43 example, artificial illumination influenced territorial singing
 44 behavior in mockingbirds (*Mimus polyglottos*); after mat-
 45 ing, male mockingbirds only sang in artificially lighted
 46 areas, or during the full moon ([91]; reviewed in [80]). In
 47 frogs, male mating calls may be disrupted by artificial
 48 lighting, and female frogs *Physalaemus pustulosus*, are less
 49 selective about mate choice and mate earlier under
 50 increased lighting levels. It has been suggested that advan-
 51 cing reproduction is a method of avoiding predation due to
 52 extended exposure under well-lit conditions (reviewed in
 53 [80]). Black-tailed godwits (*Limosa l. limosa*) based their
 54 choices of nesting sites according to roadway lighting,
 55 choosing to nest approximately 300 m away from artificial
 56 roadway lighting (reviewed in [80]). Such disruptive effects
 57 of artificial lighting even extend into invertebrate animal
 58 classes. Female glowworms, for example, attract males with
 59 visual flashes that are less visible in lighted environments
 60 (reviewed in [80]). Interruptions in such critical reproduc-
 61 tive 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 jamaicensis*) [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]. Simi-
 lar 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 nilssonii*) in Sweden are attracted to illumi-
 nated 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 migra-

tion [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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Start new paragraph	┌	┌
No new paragraph	┐	┐
Transpose	└┐	└┐
Close up	linking ○ characters	Ⓞ
Insert or substitute space between characters or words	/ through character or ∧ where required	Υ
Reduce space between characters or words		↑