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EDITORIAL

How good is the evidence that light at night can affect human health?

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Light pollution and exposure to artificial light at night (ALAN) have become almost universal in the modern world. Although there is an ongoing debate about how such environmental changes can affect human well-being and health, there is no doubt that ALAN perturbs the circadian clock – an ancestral system which synchronizes bodily physiology with the day-night cycle. The eye, especially the retina, has a dual role in this story – on the one hand, it is the unique source of light entry to the central clock in the brain, and on the other, eyes themselves are strongly regulated by endogenous circadian clocks. This editorial gives a very brief overview of the situation and poses certain unanswered questions.

Humans live in an increasingly illuminated world. The last century has seen an unprecedented increase in the use of *a*rtificial *l*ight *at n*ight (ALAN), with a current ongoing increase rate of more than 6% per year. Over 80% of the world's population, with ~ 99% in Europe and North America, lives under a "lit sky" at night (1). This exposure to nocturnal illumination outdoors is in parallel to interior domestic and industrial lighting. Many countries are now debating the impact and consequences of ALAN not only upon society but also for the environment. One of the pivotal aspects concerns perturbation of the circadian network by ALAN. Virtually all living organisms including humans have evolved an intricate system enabling their physiology and behavior to be pro-actively aligned with the predictable alternating day-night cycle, the so-called circadian clock. The importance of this finely balanced system for well-being and survival cannot be over-emphasized, and scientific pioneers in this field received the 2017 Nobel Prize for Physiology and Medicine. The eye actually plays a double role in this context: on the one hand, in mammals including humans, it is the unique entry point of light information necessary to synchronize the master circadian clock located in the hypothalamus with the environmental light-dark cycle (2); and on the other, like all organs, the eye also possesses its own endogenous circadian clocks which are important in regulating many local functions such as photoreceptor function and turnover, visual sensitivity, and intraocular pressure (3). One of the best studied phenomena under light and circadian control is the rhythmic secretion of melatonin. Melatonin is a potent neurohormone which not only facilitates sleep but also possesses anti-oxidative properties. Through a light-activated inhibitory pathway between the circadian clock and downstream neurons, there is a nocturnal surge in melatonin secretion and release into the bloodstream and cerebrospinal fluid; exposure to light during the night suppresses melatonin production (4). It is relatively easy to understand how the circadian system, which has evolved throughout > 99% of geological time under bright days alternating with dark nights, can be "confused" by exposure to artificial light at a time (evening/night) when it is not present naturally. It has been shown conclusively that in a normal domestic setting, ALAN levels are sufficient to delay onset and/or reduce melatonin secretion, especially in children due to their transparent lenses permitting higher light transmission (5). It is hypothesized that ALAN-induced perturbation of the circadian clock,

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including disruption of melatonin secretion, is very likely involved not only in short-term problems such as decreased drowsiness, sleep quality, and decreased total sleep time but also in longer-term issues like cancer, mental health, cognitive performance, obesity and weight gain, type 2 diabetes and coronary heart disease (coronary ischemia and myocardial infarction), and possible effects on dyslipidemia, arterial hypertension, and ischemic stroke (6, 7). Much less investigated are any direct effects of ALAN upon ocular health, which could also be of two non-mutually exclusive types: either through phototoxicity (light damage) to photoreceptors or via perturbation of the ocular circadian system which would then impact a wide range of processes. For example, a single night of moderate light exposure in diurnal rodents leads to widespread alteration in expression of circadian clock genes, "output" genes involved in phototransduction, and cellular activities like rhythmic photoreceptor phagocytosis (8). Furthermore, phototoxicity itself is partly under circadian control, since exposure of rats to intense light is more injurious when performed at night than during the day (9).

Light-emitting diodes (LEDs) represent a revolution in lighting technology, due notably to the lower energy consumption, and are currently replacing all other forms of lighting, in domestic, industrial, and urban settings. Due to their higher emissions in the shorter ("blue") wavelengths, at least for the lamps with a high color temperature (>4500 K), there is a risk that LEDs may exacerbate some of these problems, since the circadian clock is extremely sensitive to blue light. This singular relation between blue light and circadian clocks underlies the recent widespread calls for limiting use of LED-emitting devices (smartphones, personal computers, televisions) during the evening.

Hence, there are numerous reasons to suspect that exposure to ALAN will have repercussions for human well-being and health, but the situation remains controversial and hotly debated among scientists, healthcare professionals, and industrialists. Are the animal models suitable for informing human health? Are the light levels typically encountered by the average person at night sufficient to cause problems? Do particular populations (children, nightshift workers, pregnant women) run any heightened risks? These questions will be difficult to address fully, but the potentially far-reaching effects on industrialized society, especially in the long term, represent compelling arguments for separating the true from the false.

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