

9-1-2013

Adverse health effects of nighttime lighting: comments on american medical association policy statement.

Richard G Stevens

George C Brainard

David E Blask

Steven W Lockley

Mario E Motta

Let us know how access to this document benefits you

Follow this and additional works at: <https://jdc.jefferson.edu/neurologyfp>

Recommended Citation

Stevens, Richard G; Brainard, George C; Blask, David E; Lockley, Steven W; and Motta, Mario E, "Adverse health effects of nighttime lighting: comments on american medical association policy statement." (2013). *Department of Neurology Faculty Papers*. Paper 65.
<https://jdc.jefferson.edu/neurologyfp/65>

Adverse Health Effects of Nighttime Lighting

Comments on American Medical Association Policy Statement

Richard G. Stevens, PhD, George C. Brainard, PhD, David E. Blask, PhD, MD,
Steven W. Lockley, PhD, Mario E. Motta, MD

Abstract: The American Medical Association House of Delegates in June of 2012 adopted a policy statement on nighttime lighting and human health. This major policy statement summarizes the scientific evidence that nighttime electric light can disrupt circadian rhythms in humans and documents the rapidly advancing understanding from basic science of how disruption of circadian rhythmicity affects aspects of physiology with direct links to human health, such as cell cycle regulation, DNA damage response, and metabolism. The human evidence is also accumulating, with the strongest epidemiologic support for a link of circadian disruption from light at night to breast cancer. There are practical implications of the basic and epidemiologic science in the form of advancing lighting technologies that better accommodate human circadian rhythmicity.

(Am J Prev Med 2013;45(3):343–346) © 2013 American Journal of Preventive Medicine

Electric Lighting in the Modern World

The American Medical Association (AMA) House of Delegates in June of 2012 adopted a policy statement on nighttime lighting and human health.¹ The Executive Summary states:

Biological adaptation to the sun has evolved over billions of years. The power to artificially override the natural cycle of light and dark is a recent event and represents a man-made self-experiment on the effects of exposure to increasingly bright light during the night as human societies acquire technology and expand industry.

Circadian Rhythms

Circadian biology is the study of daily rhythms in physiology, metabolism, and behavior. These daily rhythms are endogenous—spontaneously generated by a pacemaker in the suprachiasmatic nuclei—and expressed as such in that if a person is put into a constant dark environment with no other time cues, that person will exhibit approximately 24-hour rhythms in

sleep/wake, food intake, body temperature, melatonin production, and a vast array of other physiologic and metabolic parameters for the rest of their natural lives. The endogenous rhythm is slightly longer than 24 hours in most people, and must therefore be able to be reset by exposure to the solar cycle of light and dark to remain at precisely 24 hours. Exposure of the eyes to bright light during the night, which was extremely uncommon before electricity, can disrupt this endogenous rhythmicity.

For a long time, circadian rhythmicity was viewed as an interesting phenomenon but without any important implications for human health. In the past decade, that view has changed dramatically. It is now apparent that circadian rhythmicity is central to the biology of virtually all organisms on the planet. This is not surprising given the primordial dominance of the 24-hour solar cycle over life on Earth.

The Executive Summary of the AMA report¹ continues:

The primary human concerns with nighttime lighting include ... potential carcinogenic effects related to melatonin suppression, especially breast cancer. Other diseases that may be exacerbated by circadian disruption include obesity, diabetes, depression and mood disorders, and reproductive problems.

These may seem to be bold statements by the AMA, but they are not without substantial scientific support that has been building for several decades. Exposure to bright light after sunset is an entirely unnatural occurrence that confuses our internal regulation and how we interact with the external environment. Light exposure at

From the University of Connecticut Health Center (Stevens), Farmington, Connecticut; Thomas Jefferson Medical College (Brainard), Philadelphia, Pennsylvania; Tulane University School of Medicine (Blask), New Orleans, Louisiana; and Division of Sleep Medicine, Department of Medicine (Lockley), Harvard Medical School, Council on Science and Public Health (Motta), Tufts Medical School, Boston, Massachusetts

Address correspondence to: Richard G. Stevens, PhD, University of Connecticut Health Center, 263 Farmington Ave., Farmington CT 06030-6325. E-mail: bugs@uchc.edu.

0749-3797/\$36.00

<http://dx.doi.org/10.1016/j.amepre.2013.04.011>

night triggers daytime biology, disrupting sleep, hormone regulation, and metabolism, and abolishes the darkness essential for regulating our circadian clock.

Pertinent to understanding human health risks are the remarkable new scientific advances that have been made in understanding how our endogenous circadian system detects light (blue light is the most disruptive at night, red the least),² and how the small number of circadian clock genes have a direct impact on a large proportion of our entire genome.³ It is becoming increasingly evident that circadian rhythmicity is crucial to overall health, including control of metabolism (how we process the food we eat)⁴; DNA damage response (how we are protected from radiation and toxic chemicals)⁵; and hormone production and cell cycle regulation (both affecting how we grow and develop and how our tissues are kept functional).^{6,7}

Definition of “Circadian Disruption”

A definition of “circadian disruption” is important for exposure assessment in the conduct of epidemiologic studies. But what is meant by circadian disruption? The definition is evolving, but in the present context it means a perturbation of the endogenous circadian rhythmicity, particularly by electric light exposure of the eyes during the night. Circadian rhythmicity includes both phase and amplitude characteristics of biologic markers that exhibit an endogenous, approximately 24-hour rhythm, such as circulating melatonin, circadian gene expression, and sleep. The term *circadian disruption* includes disturbances such as phase shifts of the entire circadian system, the displacement of sleep relative to the circadian clock, and/or the acute suppression of nocturnal melatonin production whether or not a phase shift also occurs. All these disruptions can be elicited by ocular light exposure at night.

Light Exposure at Night and Circadian Disruption

Melatonin is the biochemical signal of darkness—it is only produced during the night, regardless of whether an organism is day-active or night-active—and is found in some form in most eukaryotes. In 1980, the seminal observation was published that electric light during the night suppresses melatonin production in humans⁸; melatonin is a marker of circadian rhythmicity and also has important effects on it.⁹ Prior to that time, it was thought that light had little or no effect on melatonin production in humans unlike other mammals that had been examined.¹⁰ The light used in these experiments on six volunteers was bright, so it was concluded by many that only bright light could have any effect. Since then, however, abundant evidence has demonstrated that,

depending on the exposure parameters, dim light can also inhibit melatonin synthesis.

In fact, there is now a range of observations on light at night in humans¹ that show (1) bright light suppresses melatonin production in all sighted people so far tested; (2) there is a dose response in that, the brighter the light, the greater the suppression of melatonin; (3) shorter wavelengths (e.g., blue) are more effective than longer wavelengths (e.g., red) for regulating neuroendocrine, circadian, and neurobehavioral responses in humans; and (4) there are differences among people in sensitivity to light exposure at night. The physiology by which the circadian system perceives light is one of the most intriguing discoveries of modern biology; although the retina is required, an entirely new type of photoreceptor, the melanopsin-containing ganglion cell, is central to the process.¹¹

Recent research in human volunteers has focused on real-world and practical consequences of exposure to light at night on circadian rhythmicity and health. Studies^{12,13} have now demonstrated that the lighting levels typically found in the home in the evening, or emitted from computer screens and electronic tablets, can suppress melatonin secretion and affect alertness and cognitive performance.

The impact of light on sleep is also of concern, with both sleep disruption and circadian disruption contributing to metabolic disorders and other health problems in humans.¹⁴ Their relative impacts have not yet been disentangled. This distinction is important because although darkness at night is required for preservation of melatonin production and maintenance of circadian rhythmicity, sleep is not. It may be normal to awake for a period during the middle of the night,¹⁵ but as long as one remains in the dark, this will not, by itself, cause circadian disruption.

Therefore, disruption of circadian rhythmicity and sleep from the indiscriminate use of electric light at night may well increase risk of many of the diseases of modern life, including not only certain cancers¹⁶ but also obesity, diabetes, and psychiatric disorders.¹⁷ There is also emerging evidence that lighting, sleep, and circadian disruption may affect prognosis in the treatment and therapy setting.¹⁸

The Animal Model

For investigation of hazards to human health, intervention trials are obviously unethical, and so observational epidemiology is the only viable method for accumulating evidence directly on humans with which to eventually make a determination of causality. That evidence has been accumulating, indicating a connection of light at

night and circadian disruption to breast cancer risk and to a lesser extent other cancers and other chronic diseases.¹

Another important component of the evidence base for determinations of causality is an animal model. The model conceived and utilized by Blask and colleagues¹⁹ is as close as ethically possible to a direct test of the impact of light exposure at night on growth of breast cancer in women. A human breast cancer xenograft was grown in a nude rat; this tumor was then perfused with blood taken from young women at night either in the dark or after exposure to light. The effects of these blood samples, taken in dark or after light exposure, were dramatically different; the sample taken during dark virtually stopped the growth of the human tumor, whereas the sample taken after light exposure did not slow the tumor growth at all. This remarkable experimental model has far-ranging application and could be utilized for investigation of a vast array of other exposures, both chemical and physical, on growth of human cancers.

Genetics and Epigenetics

Only recently has research begun on the potential role of polymorphisms in circadian genes in disease etiology, particularly cancer.²⁰ This work may, or may not, lead to some therapeutic or screening benefits in the future. More pertinent to the general population, however, is the possibility that environmental exposures to circadian disruptors, particularly light at night, might alter expression of circadian genes by, for example, changes in promoter methylation. The first such report²¹ was of promoter hypomethylation of *CLOCK*, and hypermethylation of *CRY2* in night-working women compared to day workers based on a small sample of subjects. This area deserves expansion and emphasis.

Recommendations

There are specific recommendations that come from the emerging recognition of the importance of maintaining robust circadian rhythmicity in our daily lives.

The conclusion of the Executive Summary¹ is as follows:

Due to the nearly ubiquitous exposure to light at inappropriate times relative to endogenous circadian rhythms, a need exists for further multidisciplinary research on occupational and environmental exposure to light-at-night, the risk of cancer, and effects on various chronic diseases.

The AMA goes a step further in the report's recommendations and, based on existing evidence,

recognizes that exposure to excessive light at night, including extended use of various electronic media, can disrupt sleep or exacerbate sleep disorders, especially in children and adolescents. This effect can be minimized by using dim red lighting in the nighttime bedroom environment.

The AMA also supports the need for

developing lighting technologies at home and at work that minimize circadian disruption, while maintaining visual efficiency.

In 2007, the International Agency for Research on Cancer concluded that "shiftwork that involves circadian disruption is probably carcinogenic to humans (Group 2A)."²² Studies of shift work and breast cancer conducted since that time generally support and extend this finding.²³ Elevated breast cancer risk in shift-working women was the first prediction of the Light-at-Night theory to be extensively tested.¹⁶

But it is also clear that not all shift-work systems and schedules are equally disruptive to circadian rhythmicity and health.²⁴ This finding offers the opportunity for intervention and mitigation of the adverse health effects of circadian disruption by optimizing shift systems, and by lighting the workplace in a way that minimizes circadian disruption throughout the shift schedule. In modern societies, day workers are also exposed to ample electric lighting during the night (dusk to dawn), and this too can disrupt circadian rhythmicity in hormone secretion and in clock gene function. Therefore, there are many opportunities for reducing light during the night that will improve general well-being whether or not a scientific consensus eventually emerges that this would also lower cancer risk.

Now, the AMA has taken this issue an important step further. Given the large and expanding use of electric light throughout the world, its potential impact on human circadian rhythmicity, and the central role played by circadian physiology in health and well-being, these concerns should be addressed through both a reduction in use of unnecessary lighting and technology solutions to ensure that we can use lighting that optimizes visual performance while minimizing circadian disruption. The impact of altered lighting on health may be especially important to children, both because they are growing rapidly and because of all the new light-emitting electronic devices available today.²⁵ The time has come for this body of scientific evidence on electric light effects on circadian rhythmicity, and knowledge of the potential for harm to human health, to fully enter the domains of medicine and public health.

This work was supported in part by The Institute for Integrative Health (GCB) and in part by grant 1R21CA129875 from the National Cancer Institute to DEB. This work was also supported by the National Space Biomedical Research Institute through grant NASA NCC 9-58 to GCB and SWL. The authors appreciate the support and advice of the Council of Science and Public Health of the American Medical Association.

No financial disclosures were reported by the authors of this paper.

References

1. Council on Science and Public Health Report 4. Light pollution: adverse health effects of nighttime lighting. American Medical Association House of Delegates Annual Meeting. June 2012, Chicago IL.
2. Brainard GC, Hanifin JP, Greeson JM, et al. Action spectrum for melatonin regulation in humans: evidence for a novel circadian photoreceptor. *J Neurosci* 2001;21:6405–12.
3. Takahashi JS, Hong HK, Ko CH, McDearmon EL. The genetics of mammalian circadian order and disorder: implications for physiology and disease. *Nat Rev Genet* 2008;9:764–75.
4. Bellet MM, Sassone-Corsi P. Mammalian circadian clock and metabolism—the epigenetic link. *J Cell Sci* 2010;123(Pt 22):3837–48.
5. Sancar A, Lindsey-Boltz LA, Kang TH, Reardon JT, Lee JH, Ozturk N. Circadian clock control of the cellular response to DNA damage. *FEBS Lett* 2010;584:2618–25.
6. Ota T, Fustin JM, Yamada H, Doi M, Okamura H. Circadian clock signals in the adrenal cortex. *Mol Cell Endocrinol* 2012;349:30–7.
7. Hunt T, Sassone-Corsi P. Riding tandem: circadian clocks and the cell cycle. *Cell* 2007;129:461–4.
8. Lewy AJ, Wehr TA, Goodwin FK, Newsome DA, Markey SP. Light suppresses melatonin secretion in humans. *Science* 1980;210:1267–9.
9. Blask DE. Melatonin, sleep disturbance and cancer risk. *Sleep Med Rev* 2009;13:257–64.
10. Brainard GC, Hanifin JP. Photons, clocks, and consciousness. *J Biol Rhythms* 2005;20:314–25.
11. Provencio I. The hidden organ in your eyes. *Sci Am* 2011;304:54–9.
12. Gooley JJ, Chamberlain K, Smith KA, et al. Exposure to room light before bedtime suppresses melatonin onset and shortens melatonin duration in humans. *J Clin Endocrinol Metab* 2011;96:E463–E472.
13. Cajochen C, Frey S, Anders D, et al. Evening exposure to a light-emitting diodes (LED)-backlit computer screen affects circadian physiology and cognitive performance. *J Appl Physiol* 2011;110:1432–8.
14. Cappuccio FP, Miller MA, Lockley SW, eds. *Sleep, health and society: from aetiology to public health*. Oxford, UK: Oxford University Press, 2010.
15. Wehr TA. In short photoperiods, human sleep is biphasic. *J Sleep Res* 1992;1:103–7.
16. Stevens RG. Light at night, circadian disruption, and breast cancer: assessment of existing evidence. *Int J Epidemiol* 2009;38:963–70.
17. Stevens RG, Blask DE, Brainard GC, et al. Meeting Report: The role of environmental lighting and circadian disruption in cancer and other diseases. *Environ Health Perspect* 2007;115:1357–62.
18. Kamdar BB, Needham DM, Collop NA. Sleep deprivation in critical illness: its role in physical and psychological recovery. *J Intensive Care Med* 2012;27:97–111.
19. Blask DE, Brainard GC, Dauchy RT, et al. Melatonin-depleted blood from premenopausal women exposed to light at night stimulates growth of human breast cancer xenografts in nude rats. *Cancer Res* 2005;65:11174–84.
20. Zhu Y, Brown HN, Zhang Y, Stevens RG, Zheng T. Period3 structural variation: a circadian biomarker associated with breast cancer in young women. *Cancer Epidemiol Biomarkers Prev* 2005;14:268–70.
21. Zhu Y, Stevens RG, Hoffman AE, et al. Epigenetic impact of long-term shiftwork: pilot evidence from circadian genes and whole-genome methylation analysis. *Chronobiol Int* 2011;28:852–61.
22. Straif K, Baan R, Grosse Y, et al. Carcinogenicity of shift-work, painting, and fire-fighting. *Lancet Oncol* 2007;8:1065–6.
23. Jia Y, Lu Y, Wu K, et al. Does night work increase the risk of breast cancer? A systematic review and meta-analysis of epidemiological studies. *Cancer Epidemiol* 2013;37:197–206.
24. Bamba CL, Whitehead MM, Sowden AJ, Akers J, Petticrew MP. Shifting schedules: the health effects of reorganizing shift work. *Am J Prev Med* 2008;34:427–34.
25. Stevens RG. Does electric light stimulate cancer development in children? *Cancer Epidemiol Biomarkers Prev* 2012;21:701–4

Did you know?

The *AJPM* Most Read and Most Cited articles are listed on our home page.
Go to www.ajpmonline.org.