

Environmental Factor

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Light and disruption of sleep cycles explored at NTP workshop

By Kelly Lenox

The National Toxicology Program (NTP) assembled an international panel of experts at NIEHS March 10-11 to discuss how disruptions to circadian rhythms, or natural sleep-wake cycles, affect health.

The scientific input gathered during the day-and-a-half meeting will help NTP inform its literature-based assessments of health effects associated with changes in light exposures, including light at night and studies of shift work.

The impact of a 24/7 society

Circadian disruptions addressed at the workshop include the following.

- Exposures to light at night, including use of electronic devices at night and urban light pollution.
- The complex scenario of shift work, which can involve interruptions in light-dark cycles and changes in sleep patterns.
- Changes in the timing of exposures to natural light, including jet lag.

Nearly all tissues in the human body have clocks that determine when certain genes are active, according to Fred Turek, Ph.D., from Northwestern University, who presented an overview. Times of activity vary among organs and among cell types within organs.

"I don't know of any disease process, whether it's Alzheimer's, or cardiovascular, or diabetes, or neurological disorders ... in which shift workers do not show a higher preponderance of the disorder than non-shift workers," he said.

Studying cancer and noncancer outcomes

Organizers will use workshop discussions to inform two activities. The NTP Office of the Report on Carcinogens (ORoC), led by Ruth Lunn, Dr.P.H., will conduct a health hazard assessment, focusing on cancer.

The NTP Office of Heath Assessment and Translation (OHAT), led by Kris Thayer, Ph.D., will look at noncancer outcomes, through a systematic review of scientific literature. Lunn and Windy Boyd, Ph.D., from OHAT, co-organized the workshop.

"We're interested in light and sleep as exposures, so this work is a departure from our usual approach to studying a chemical or mixture," Boyd said. Both the direct effects of exposures to light and effects of activities enabled by light, such as shift work, are of potential concern.



"We are the only species that does not listen to our clock," Turek said. (Photo courtesy of Steve McCaw)



"We live in a 24/7 society," said Lunn, shown center, with, from left, Thayer and Boyd. (Photo courtesy of Steve McCaw)

“One of the virtues of gathering these folks together in the same room was hearing from experts who have studied different aspects of our overall questions,” Lunn said. “We received excellent input to guide our next steps.”

Defining the scope of the literature-based analyses

Participants provided input on NTP efforts to define the scope of the literature-based evaluations, including defining the topic, identifying the most relevant types of studies, and selecting approaches to synthesize across studies. “This problem formulation work is a necessary step in designing systematic reviews of the literature,” said Thayer.

Circadian rhythms must be defined before scientists can address circadian disruptions, participants noted. Factors involved in circadian disruption may vary, depending on the health outcome of interest.

Moreover, as Michael Gorman, Ph.D., from the University of California at San Diego, pointed out, circadian rhythms vary with the seasons. He cited differences in reproductive, immune, and metabolic systems in winter compared with summer.

Along with definitions, standardization is necessary. Several commenters addressed design of animal studies. For instance, published papers generally lack data on light intensity, wavelength, and angle. In addition, species selection should consider that production of and sensitivity to melatonin varies across species, as does sensitivity to light. Both nocturnal and diurnal models should be considered. All of these factors affect the human relevance of animal studies.

Data needs

Janet Hall, M.D., from the NIEHS Clinical Research Branch, moderated the closing discussion on research opportunities. “What are some of the things that can be handled in the short term that will enable better studies?” she asked, mentioning both standardization and identification of biomarkers.

OHAT will present a document outlining its rationale for the literature-based review of noncancer outcomes at a December advisory board meeting. ORoC will use input from the meeting to develop methods for conducting its review of cancer outcomes. Overviews of studies related to the topic are available on the [workshop web page \(http://ntp.niehs.nih.gov/pubhealth/roc/candidates/meetings/workshop_alan.html\)](http://ntp.niehs.nih.gov/pubhealth/roc/candidates/meetings/workshop_alan.html).

Electronic screens

Society’s growing concern with light at night, especially from electronic screens, was reinforced shortly after the workshop when Apple released a software update with an optional setting called Night Shift.

Between sunset and sunrise, the setting reduces emissions of blue light from device screens. Apple said studies have shown that evening exposure to bright blue light can affect circadian rhythms and make it harder to fall asleep.



Roel Vermeulen, Ph.D., left, from Utrecht University in The Netherlands, seated by Johnni Hansen, Ph.D., from the Danish Cancer Society, stressed the need for public education so people can make healthy choices, as with cigarette smoking. (Photo courtesy of Steve McCaw)



Mariana Figueiro, Ph.D., right, is program director of the Lighting Research Center at Rensselaer Polytechnic Institute. Andrew Coogan, Ph.D., directs the National University of Ireland Chronobiology and Sleep Research Laboratory. (Photo courtesy of Steve McCaw)



Gorman, right, listened to comments from David Blask, M.D., Ph.D., left, a leader of the Circadian Cancer Biology Group at Tulane University School of Medicine. (Photo courtesy of Steve McCaw)



Hall, right, seated next to Richard Stevens, Ph.D., from the University of Connecticut, led the session on research needs. "We've had an incredibly rich discussion so far," she said. (Photo courtesy of Steve McCaw)

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