Report on Workshop: Shift Work at Night, Artificial Light at Night, and Circadian Disruption

NTP Board of Scientific Counselors Meeting
June 15-16, 2016

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Outline

- Background information
- Workshop objectives and format
- Workshop outcomes: Issues and discussions
- NTP evaluations: Next steps
NTP’s Interest in Shiftwork, LAN & Circadian Disruption

• **Light at night (LAN)** nominated to ORoC (cancer) and OHAT (non-cancer outcomes)
  
  – IARC concluded that “**shiftwork that involves circadian disruption**” is probably carcinogenic to humans (Group 2A)

• NTP solicited public comment on “**shiftwork involving light at night**” (January 2012)

• ORoC presented concept at June 2013 BSC meeting “**Shift Work at Night, Light at Night, and Circadian Disruption**”
  
  – Workshop or webinar was proposed in the concept
How to evaluate health hazards

Strategies for synthesizing evidence across a large, complex database

Environmental disruptors
- Shift work
- Phase shift/jet lag
- LAN
- Sleep disruption
- Meal timing

Biomarkers of circadian disruption
- Hormones
- Clock gene changes
- Epigenetic effects

Adverse health outcomes?
- Cancer
- Non-cancer

Human epidemiological studies of health outcomes

Animal models, mechanistic studies: humans, animals, in vitro

Strategies for synthesizing evidence across a large, complex database
Stepwise approach leading up to meeting

- Identify non-cancer outcomes
- Identify scope of the literature
- Obtain input on strategies to conduct the health hazard evaluations
- Identify data gaps and research needs

Cardiovascular, metabolic, reproductive, gastrointestinal, immunological, and neurological outcomes

Session abstracts: Overview of human and animal studies

Workshop discussion
Workshop Format

- 6 successive sessions
  - Circadian disruption (session 1)
  - Exposure scenarios - light, shift work, sleep and other exposures (sessions 2 to 4)
  - Strategies for conducting the cancer hazard evaluation (session 5)
  - Data gaps and research needs (session 6)

- Session format:
  - Panel presentations (sessions 1 to 3) related to state of the science
  - Moderator-led discussions related to advancing the science

- March 10 (afternoon) to 11, 2016

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<tr>
<th>Name</th>
<th>Institution/Institutional Position</th>
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<td>David Blask, PhD, MD</td>
<td>Tulane University</td>
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<td>Andrew Coogan, PhD</td>
<td>Maynooth University, Ireland</td>
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<td>Mariana Figueiro, PhD</td>
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Workshop Outcomes

• Input on conducting the NTP health hazard evaluations
  – Suggested light as unifying factor as it is both an effector and enabler
  – Identified information and issues relevant for evaluating studies and protocol development

• Data gaps and research needs for the field
  – Suggestions for characterizing exposures and study designs

• Studies on interventions
Light as an effector and enabler

- Electric light as an effector
  - Direct effects on circadian disruption and nocturnal melatonin suppression

- Electric light as an enabler
  - Paved the way for individuals to eat, sleep, and conduct other activities 24/7

- Shift work: light as an effector and enabler, as it is a complex exposure scenario

NASA Earth Observatory image of the city lights across the continental U.S. in 2012 via partnership between NASA, NOAA, and DoD
Health consequences of electric lighting practices in the modern world

Impact on monograph development

• Reasonable to consider all studies related to light in the same monograph because of the overlapping nature of the exposures

• Separate assessments (or conclusions) will likely be conducted for studies evaluating direct effects of light vs. studies evaluating effects from activities of light as enabler

• Assessments determined by nature and scope of the databases, which vary by health outcome
Issues related to evaluating studies and protocol development

• Light
  – Multiple characteristics: intensity, amount, spectrum, distribution, timing, duration, and photic history are related to circadian disruption
  – Total light exposure is important, not just LAN; light exposure during day influences night-time sensitivity

• Human studies
  – Meta-analyses not informative
  – Selection bias: “healthy shift worker survival effect”

• Animal models
  – Although don’t fully replicate complex, overlapping exposure scenarios in humans, they play a key role in understanding specific exposures, mechanisms, and provide input for intervention
  – Important to translate light metrics from animals to humans because nocturnal animals are more sensitive to light
  – Not all animals produce melatonin or have melatonin receptors
Research Needs for the Field

• Human epidemiological studies
  – Conduct field studies on light exposure using calibrated devices and detailed questionnaire data, which can be scaled up for use in large epidemiology studies
  – Collect information (questionnaire, biomarkers, etc.) that provide comprehensive characterization of shift work (e.g., scheduling and nature) as well other “exposures” such as light exposure, sleep and eating patterns

• Animal studies
  – Conduct studies on dim LAN at lower intensity and using diurnal models to more closely replicate human exposures/effects
  – Conduct preliminary studies measuring biomarkers at multiple time points to determine optimal times for larger scale studies
  – Evaluate experimentally induced diseases (e.g., using known toxicants) under different light conditions
Light and shift work are essential to our society

Experimental human studies
- Light characteristics and biomarkers of circadian disruption
- Interventions such as using blue light-blocking goggles

Studies in experimental animals
- Evaluated interventions on health outcomes
- Examples: Red light and neurological and cardiovascular disease

Red Wavelength is less Detrimental

Forced swim test for assessing depression

Bedrosian et al. 2013; Journal of Neuroscience
Nelson presentation
• Workshop report in preparation

• OHAT plans to present a concept for the December 2016 NTP BSC meeting
  – Outline research questions for review

• NTP is using input from the workshop to develop protocols for conducting health hazard evaluations

• Identify potential interventions by summarizing existing evidence
Workshop Team

• Organizers (NIEHS)
  – Windy Boyd*
  – Ruth Lunn
  – Kris Thayer

• Moderators
  – Tania Carreón-Valencia (NIOSH)
  – Claire Caruso (NIOSH)
  – Michael Twery (NHLBI)

• Rapporteurs
  – Gloria Jahnke (NIEHS)
  – Tina Lawson (NIOSH)
  – Katie Pelch (NIEHS)
  – Kyla Taylor (NIEHS)

  * Also served as a moderator or rapporteur

• Technical support
  – Andy Ewens (ILS)
  – Sandy Garner (ILS)
  – Whitney Mitchel (ICF)
  – Pam Schwingl (ILS)*
  – Courtney Skuce (ICF)

• Administrative support
  – Ella Darden (ILS)
  – Anna Lee Mosley (Kelly Services)
  – Tracy Saunders (ILS)

• Webcast support
  – Nathan Mitchiner (NETE Solutions)

• NTP Web Team