Update from the National Toxicology Program's Workshop on Electric Light-Related Exposures

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Outline

Background on NTP, ORoC, and OHAT

NTP’s interest in electric light-related exposures

NTP workshop update

Current NTP activities
Evaluates agents of public health concern

**Interagency program**
- Headquartered at the National Institute of Environmental Health Sciences (NIEHS)
- National Institute for Occupational Safety and Health (NIOSH)
- National Center for Toxicological Research (NCTR)

**Research**
- Thousands of agents evaluated in comprehensive toxicology studies

**Literature analysis activities**
- Office Report on Carcinogens (ORoC)
- Office of Health Assessment & Translation (OHAT)

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**National Toxicology Program (NTP)**

- US Department of Health and Human Services (DHHS)
  - NIH
  - CDC
  - FDA
  - NIEHS
  - NIOSH
  - NCTR

NTP’s interest in electric light-related exposures

Defining the candidate substance is a challenge

- **Light at night (LAN)** nominated to ORoC (cancer) and OHAT (non-cancer endpoints)
  - IARC concluded that “shiftwork that involves circadian disruption” is probably carcinogenic to humans (Group 2A)
  - Urged to include more than shiftwork due to widespread LAN
- ORoC solicited public comment on “shiftwork involving light at night”
  - NTP Board of Scientific Counselors endorsed concept although challenging
  - First step to identify “candidate substance”
- NTP held **public workshop** at NIEHS March 10-11, 2016
Evaluating health hazards

Strategies for synthesizing evidence across large, complex database

Environmental disruptors
- Shift work
- Phase shift/jet lag
- ALAN
- 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*
<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
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<tbody>
<tr>
<td>David Blask, PhD, MD</td>
<td>Tulane University</td>
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<td>Randy Nelson, PhD</td>
<td>The Ohio State University</td>
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<td>Andrew Coogan, PhD</td>
<td>Maynooth University, Ireland</td>
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<td>Satchin Panda, PhD</td>
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<td>Mariana Figueiro, PhD</td>
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<td>Michael Smolensky, PhD</td>
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<td>Michael Gorman, PhD</td>
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<td>Richard Stevens, PhD</td>
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<td>Johnni Hansen, PhD</td>
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<td>Roel Vermeulen, PhD, MSc</td>
<td>Utrecht University</td>
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Workshop Takeaways
World map of artificial brightness as a ratio to natural sky brightness (Falchi et al. 2016)
Clocks are everywhere

EXTERNAL CUES
- Light
- Food

CLOCK OSCILLATOR
- SCN
- extra SCN

CLOCK OUTPUT
- Melatonin
- Sleep/Wake
- Feed/Fast
- Metabolic Pathways
- Hormones

PERIPHERAL TISSUES

Endocrine or autonomic innervation
Shiftwork study design considerations

Primary shiftwork exposure metrics (1,8)

**CHRONOTYPE**

- Disturbed social pattern (1)
- Disturbed lifestyle aspects (1,3,6)
- Disturbed sleep pattern (1,2)
- Disturbed eating pattern (1,3)
- Disturbed light exposure (1,4)
- Disturbed vigilance and cognition (10,11)

**STRESS SYMPTOMS (1)**
- Reproductive factors (1,6)
- Physical activity (1,2,3)
- BMI (9)

**µ USE OF TOBACCO /ALCOHOL (1,3)**
- Melatonin (5,6)
- Circadian disruption (6)
- Uncoupling peripheral clocks (6)
- Gut microbiome (7)

**Δ DIET (1,3,6,9)**
- Light at night
  - Circadian disruption (6)
  - Melatonin (5,6)
  - Sun exposure (1,4)
  - Vitamin D

**MEASUREMENT METHODS**

- Questionnaire (1)
- Actigraphy sensor (2)
- 24-hour recall log (3)
- Light Sensor (4)
- Biomarkers: Urine (5)
- Biomarkers: Blood (6)
- Biomarkers: Feces (7)
- Employer registration data (8)
- Anthropometry (9)
- Psychomotor vigilance task (10)
- Memory tests (11)
Animal models of shiftwork

Exposure Components
- Timing of Activity
- Timing and Duration of Sleep
- Light: Dark Cycle/Light-at-Night
- Timing of Feeding

Mechanisms
- Desynchronization of Circadian Oscillators
- Disruption of Homeostasis
- Endocrine Disruption
- Increased Inflammation

Outcomes
- Cancer
- Neurobehavioral
- Cardiometabolic
- Reproductive

Factors:
- Age
- Sex
- Chronicity and Type of Exposure
- Circadian Phenotype
- Background Photic Exposure
Proposed title: *Health consequences of electric lighting practices in the modern world*
• Increase visibility of pervasive exposures and potential health effects
  – >150 attendees, in person or via webinar
  – Videos of presentations and discussions available
    • [http://ntp.niehs.nih.gov/go/workshop_ALAN](http://ntp.niehs.nih.gov/go/workshop_ALAN)
    – Workshop report to be submitted for publication early 2017
• Follow up on new research activities identified at workshop
• ORoC health hazard evaluation of cancer outcomes in progress
  – Separate assessments of human data for each exposure scenario
    • Night shift work, light exposures, transmeridian travel
    • Social jet lag, use of consumer electronics
  – Also summarize biomarker studies of circadian disruption in humans

• Considerations for OHAT non-cancer evaluations
  – French ANSES report on night shift work
  – Compelling evidence in experimental models but lack of epidemiological studies
• Need better measures of light, not just satellite data
  – Validation of detailed questionnaires
• Lack of epidemiological evidence of light effects
  – Add measures of light exposures to large cohort studies
• Lack of biomarkers of exposure and effects
• Need to compare diurnal animal models to nocturnal animals
  – Also melatonin-sufficient models
• Evaluate experimentally-induced diseases (e.g. exposures to known toxicants) under different light conditions
• 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

• 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
Questions/Comments?

http://ntp.niehs.nih.gov/go/workshop_ALAN