The Dark Side of Light at Night
The rhythm of life

Environment
- Shift work
- Sleep restriction
- Time-zone travel
- Social jet lag
- Western diet

Ageing
- Maternal program
- Development
- Ontogeny of neural and peripheral clocks

Immune cells
Inflammation

Liver
Skeletal muscle
Insulin sensitivity

Adipose tissue
Fat accumulation

CNS
Reward
Learning
Mood
Arousal

Pancreas
Insulin secretion

Heart
Vascular tissue
Kidney
Cardiovascular function

Intestine
Food absorption

Maynooth University
National University of Ireland Maynooth
Master circadian clock
Circadian rhythms
Circadian photoreceptors
Clocks, clocks, everywhere...
Buttgereit, Smolen, Coogan and Cajochen, Nature Re. Rheum. 2015
The Suprachiasmatic nuclei (SCN) region is located in the hypothalamus of the brain.

The SCN sends signals throughout the body in response to light and dark.

Mood Status:

- Happy
- Neutral
- Sad
- Angry
Light-at-night
Light-at-night
Sources of light-at-night
Sources of light-at-night
Sources of light-at-night
Light-at-night and cancer incidence

Kloog et al, 2010
**Table 2.** OR of Variables Affecting Breast Cancer Risk in Israeli Women (Binary Logistic Regression) 10 to 15 Years Before Diagnosis.†

<table>
<thead>
<tr>
<th>Variable</th>
<th>P Value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep duration</td>
<td>.03</td>
<td>0.74 (0.57-0.97)</td>
</tr>
<tr>
<td>Reading with bed light illumination before retiring to sleep</td>
<td>.02</td>
<td>0.81 (0.67-0.97)</td>
</tr>
<tr>
<td>Sleeping with closed shutters during the night</td>
<td>.04</td>
<td>0.82 (0.68-0.99)</td>
</tr>
<tr>
<td>Resides near strong ALAN sources</td>
<td>.01</td>
<td>1.52 (1.10-2.12)</td>
</tr>
</tbody>
</table>

Abbreviations: OR, odds ratio; ALAN, artificial light at night.
†Based on a sample of n = 93 cases and 188 controls.

**Table 3.** Hierarchical Binary Logistic Regression Analysis of Variables Affecting Breast Cancer Risk in Israeli Women, 10 to 15 Years Before Diagnosis.†

<table>
<thead>
<tr>
<th>Step</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\chi^2$</td>
<td>5.28*</td>
<td>10.91*</td>
<td>36.57***</td>
</tr>
<tr>
<td>Nagelkerke $R^2$</td>
<td>0.03</td>
<td>0.05</td>
<td>0.17</td>
</tr>
<tr>
<td>Cox and Snell $R^2$</td>
<td>0.02</td>
<td>0.04</td>
<td>0.12</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Exp (B)</th>
<th>Wald</th>
<th>Exp (B)</th>
<th>Wald</th>
<th>Exp (B)</th>
<th>Wald</th>
</tr>
</thead>
<tbody>
<tr>
<td>Place of birth (in/out of Israel)</td>
<td>0.54</td>
<td>5.31*</td>
<td>0.54</td>
<td>5.14*</td>
<td>0.65</td>
<td>2.21</td>
</tr>
<tr>
<td>Sleep duration</td>
<td>0.76</td>
<td>4.79*</td>
<td>0.74</td>
<td>4.64*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>The number of times awoken at night</td>
<td>0.99</td>
<td>0.003</td>
<td>1.09</td>
<td>0.32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subjective sleep quality</td>
<td>0.89</td>
<td>0.94</td>
<td>1.00</td>
<td>0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subjective light intensity in the bedroom during the night</td>
<td>1.21</td>
<td>0.78</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleeping with light at the intensity for reading</td>
<td>0.96</td>
<td>0.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reading with room light illumination before retiring to sleep</td>
<td>0.96</td>
<td>0.17</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reading with bed light illumination before retiring to sleep</td>
<td>0.81</td>
<td>5.23*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Falling asleep with the TV on</td>
<td>0.84</td>
<td>1.80</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Falling asleep with the TV on for most of the night</td>
<td>1.26</td>
<td>1.91</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleeping with light penetrating the room from outside</td>
<td>0.96</td>
<td>0.16</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleeping with dim light during the night</td>
<td>0.89</td>
<td>0.82</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleeping with closed shutters during the night</td>
<td>0.82</td>
<td>4.23*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Turning the lights on when waking up during the night</td>
<td>0.88</td>
<td>1.69</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residing near strong ALAN sources</td>
<td>1.52</td>
<td>6.33**</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of bedroom illumination: LWL/SWL</td>
<td>1.35</td>
<td>0.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of bed light illumination: LWL/SWL</td>
<td>1.56</td>
<td>0.64</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Keshett-Sitton et al, 2015
Circadian desynchrony and metabolic dysfunction; did light pollution make us fat?

C.A. Wyse⁻¹, C. Selman, M.M. Page, A.N. Coogan, D.G. Hazlerigg

⁻¹Institute of Biological and Environmental Sciences, University of Aberdeen, Aberdeen, AB24 3TZ, UK
⁻²Department of Psychology, National University of Ireland, Maynooth, Co Kildare, Ireland

(A) % Country Electrified vs. Prevalence of Obesity (≤ Adult Males with BMI > 26)

(B) Mean UK Male BMI vs. Artificial Light Exposure

Mean Body Mass Index vs. Trillion Lumen Hours
Outdoor artificial light at night, obesity, and sleep health: Cross-sectional analysis in the KoGES study

Yong Seo Koo, Jin-Young Song, Eun-Yeon Joo, Heon-Jeong Lee, Eunil Lee, Sang-kun Lee, and Ki-Young Jung

**Table 2.** The odds ratios for obesity in the high outdoor ALAN versus low outdoor ALAN groups.

<table>
<thead>
<tr>
<th></th>
<th>Univariate model&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Model 1&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Model 2&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds ratio for obesity (95% CI)</td>
<td>1.24 (1.14–1.35)</td>
<td>1.25 (1.14–1.37)</td>
<td>1.20 (1.06–1.36)</td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.003</td>
</tr>
</tbody>
</table>
# Light-at-Night and Depression

**Table 3**

Logistic regression analysis for the association between variables and risk of depression.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Crude OR</th>
<th>95% CI</th>
<th>P</th>
<th>Adjusted OR*</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAN (NLavg ≥ 5 vs. &lt; 5 lx)</td>
<td>1.92</td>
<td>1.17</td>
<td>3.14</td>
<td>0.01</td>
<td>1.89</td>
<td>1.10</td>
</tr>
<tr>
<td>Daytime light (DL1000 ≥ 60 vs. &lt; 60 min)</td>
<td>0.72</td>
<td>0.46</td>
<td>1.12</td>
<td>0.14</td>
<td>0.89</td>
<td>0.54</td>
</tr>
<tr>
<td>Insomnia (yes vs. no)</td>
<td>4.66</td>
<td>2.62</td>
<td>8.29</td>
<td>&lt; 0.01</td>
<td>4.17</td>
<td>2.24</td>
</tr>
<tr>
<td>Hypertension (yes vs. no)</td>
<td>1.60</td>
<td>1.03</td>
<td>2.48</td>
<td>0.03</td>
<td>1.35</td>
<td>0.84</td>
</tr>
<tr>
<td>Habitual sleep duration (per min)</td>
<td>0.996</td>
<td>0.992</td>
<td>0.999</td>
<td>0.02</td>
<td>0.996</td>
<td>0.992</td>
</tr>
<tr>
<td>Habitual physical activity (per log MET-h/week)</td>
<td>0.84</td>
<td>0.72</td>
<td>0.99</td>
<td>0.04</td>
<td>0.81</td>
<td>0.68</td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAN (NL10 ≥ 30 vs. &lt; 30 min)</td>
<td>1.77</td>
<td>1.10</td>
<td>2.87</td>
<td>0.02</td>
<td>1.71</td>
<td>1.01</td>
</tr>
<tr>
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<td>1.12</td>
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<td>1.03</td>
<td>2.48</td>
<td>0.03</td>
<td>1.35</td>
<td>0.84</td>
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<tr>
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<td>0.992</td>
<td>0.999</td>
<td>0.02</td>
<td>0.996</td>
<td>0.992</td>
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<td>0.72</td>
<td>0.99</td>
<td>0.04</td>
<td>0.82</td>
<td>0.69</td>
</tr>
</tbody>
</table>

OR, odds ratio; CI, confidence interval; LAN, light at night; NLavg, average intensity of nighttime light exposure; DL1000, duration of daytime light exposure ≥ 1000 lx; NL10, duration of nighttime light exposure ≥ 10 lx; MET, metabolic equivalent task.

* Adjusted for all covariates shown.
Chronic dim light at night provokes reversible depression-like phenotype: possible role for TNF

TA Bedrosian, ZM Weil and RJ Nelson
Effects of dim LAN on affective behaviours

Circadian rhythm monitoring

OR

Group housed

Baseline 3 weeks.

Elevated plus maze

Sucrose preference test

Tail suspension test

Forced swim test

Light-at-night/control 3 weeks.

OR
LAN and Affective Behaviours–Circadian Disruption?
LAN and Affective Behaviours

Forced swim test (latency)  Forced swim test (immobility)  Tail suspension test
LAN and hippocampal stem cell proliferation

**Control**

**LAN**

![Ki67 expressing cells graph](#)
Exposure

Mechanisms

Acute Effects

Chronic Effects

LAN

Circadian desynchronisation

Melatonin suppression

Disturbed/shortened sleep

Altered Affect

Neurocognitive effects

Adverse physical health outcomes

Adverse psychological health outcomes
Action of light at night on the circadian system
Suppression of nocturnal melatonin

Bonmatti-Carrion et al, 2014
Evening use of light-emitting eReaders negatively affects sleep, circadian timing, and next-morning alertness

Anne-Marie Changa,b,1,2, Daniel Aeschbacha,b,c, Jeanne F. Duffya,b, and Charles A. Czeislera,b

aDivision of Sleep and Circadian Disorders, Departments of Medicine and Neurology, Brigham and Women's Hospital, Boston, MA 02115; bDivision of Sleep Medicine, Harvard Medical School, Boston, MA 02115; and cInstitute of Aerospace Medicine, German Aerospace Center, 51147 Cologne, Germany
Evening use of light-emitting eReaders negatively affects sleep, circadian timing, and next-morning alertness

Anne-Marie Chang\textsuperscript{a,b,1,2}, Daniel Aeschbach\textsuperscript{a,b,c}, Jeanne F. Duffy\textsuperscript{a,b}, and Charles A. Czeisler\textsuperscript{a,b}

\textsuperscript{a}Division of Sleep and Circadian Disorders, Departments of Medicine and Neurology, Brigham and Women’s Hospital, Boston, MA 02115; \textsuperscript{b}Division of Sleep Medicine, Harvard Medical School, Boston, MA 02115; and \textsuperscript{1}Institute of Aerospace Medicine, German Aerospace Center, 51147 Cologne, Germany
Shift work
Shift Work

- Light:Dark Cycle/Light-at-Night
- Night Work
- Night Feeding
- Shortened Sleep
- Desynchronisation of circadian oscillators
- Endocrine disruption
- Homeostasis
- Immunity-Inflammation
- Neurobehavioural
- Cardiometabolic
- Cancer
- Other
Shift-workers do not entrain to work schedules

Health in a 24-h society. Rajaratnam SM, Arendt J. Lancet. 2001 Sep 22;358(9286):999-1005
Long-term consequences of shift work

Circadian rhythm disruptions
- Body temperature
- Respiratory rate
- Hormonal production
- Menstrual cycle
- Urinary excretion
- Cell division

Mental Health
- Stress
- Anxiety
- Depression
- Neuroticism
- Reduced vigilance
  *Burnout syndrome*

Brain effects
- Sleep loss
- REM sleep reduction
- Stage 2 sleep reduction
- Fatigue
- Reduced brain volume

Cardiovascular disorders
- 40% increased risk for:
  - Angina pectoris
  - Hypertension
  - Myocardial infarction

Gastrointestinal disorders
- Dyspepsia
- Heartburn
- Abdominal pains
- Flatulence

Reproductive effects
- Spontaneous abortion
- Low birth weight
- Prematurity

Increased cancer
- Breast cancer
- Colorectal cancer

Link between night shift work and breast cancer risk

<table>
<thead>
<tr>
<th>Years on night shift</th>
<th>Relative risk of breast cancer*</th>
</tr>
</thead>
<tbody>
<tr>
<td>30+</td>
<td>1.36 (36% increased risk)</td>
</tr>
<tr>
<td>1-29</td>
<td>1.08 (8%)</td>
</tr>
<tr>
<td>Never</td>
<td>1.00</td>
</tr>
</tbody>
</table>

*Note: Figures from Nurses’ Health Study. Risk adjusted for age and other contributory factors. Source: JNCI (2001)
Shift work as a risk factor for metabolic disease

Shift work

Circadian disturbance

Sleep, exercise, diet

Insulin resistance, weight gain

Type 2 diabetes

Kivimaki et al, PLoS Medicine, 2011
Questions and Future Directions

- More mechanistic studies (e.g., longitudinal animal studies).
- Better epidemiology of LAN.
- Measurement of individual exposures.
- Understanding the role of LAN in the exposure of shift work.
- Impacts on public policy (e.g., street lighting).
- Impact on industry.
- Considerations in the clinical setting.
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Michael Cleary-Gaffney
Jacinta Finn
Dr. Sean Commins
Prof Paul Moynagh
Dr. Amy Beynon
Dr. Alison Baird
Dr. Emma O’Callaghan
Dr. Cathy Wyse

Dr. John McDermott
Prof Seamus Sreenan
Dr. Ultan Healy

Prof Frank Buttgereit
Prof Johannes Thome
Prof Aurel Popa-Wagner

Dr. Bogdan Voinescu