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### **Opinion**

## Linking the non-visual effects of light exposure with occupational health

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#### Introduction

In May 2018, the Federal Institute for Occupational Safety and Health (BAuA, Germany) hosted 'Light and Health at Work', a workshop concerning occupational health issues relating to non-visual effects of light of both indoor and shift workers. The agenda reflected a common interest in translational research linking laboratory findings with occupational and public health outcomes, and resulted in the founding of the European scientific network NoVEL (standing for Non-Visual Effects of Light). This article sets out the network participants' shared goals to improve the scientific evidence about light's non-visual effects, circadian disruption and wellbeing, using light exposure interventions with high quality assessment of light.

The main work conditions that impair exposure profiles that support healthy circadian regulation are daytime indoor work that reduces light exposures and night-shift work that increases light-at-night (LAN).

#### Daytime indoor work

Daylight reduces differences in circadian rhythm phase, but indoor workers spend on average 3.5 h less outdoors on workdays.<sup>2</sup> This negative influence on circadian regulation may induce social jetlag<sup>3</sup> and, over time, have an adverse impact on health. 4-6 Potentially, this could be counteracted by increased indoor light levels or short-wavelength enriched light. 7-12 However, other reviews of light interventions highlight that there is still limited evidence of the effects of daylight exposure or of increased daytime light levels at work, and studies may not have been sufficient in size, duration, followup or range of outcome measures to elucidate the full health impacts. 13,14 This situation is particularly noticeable for workplace interventions and long-term health outcomes.

#### Night-shift work

Night work has been associated with cardiovascular disease (CVD), diabetes, impaired cognition, mental disorders and cancers, including breast cancer. <sup>15–23</sup> Several mechanisms including LAN, circadian disruption and insufficient sleep<sup>24</sup> have been put forward to link night work to adverse health effects. Light exposure interventions to mitigate the adverse effects of shift work<sup>25,26</sup> have produced mixed results. Tailored interventions based on individual characteristics, such as chronotype and age, can lead to higher participation rates and better results.<sup>27</sup>

To date, many studies lack a sufficiently rigorous exposure metrology and a basis in chronobiology to test these possibilities.<sup>28</sup> Chronobiological disruption from exposure to light can be masked in field studies that do not measure and allow for variations in individual exposures and/or the timing of the individual's internal clock.<sup>29</sup> There are similarities between the apparent effects of night-shift and early morning work and insufficient sleep,<sup>18</sup> but properly testing the possible causal mechanisms presents a substantial challenge. A co-ordinated multidisciplinary approach that meets the complex demands of the field is overdue.

The sections below illustrate important specializations that can and should be considered as part of a systematic investigation into light and health at work.

#### Non-visual effects of light

Light is perceived through five photopigments: melanopsin, rhodopsin and three cone opsins. Intrinsically-photosensitive retinal ganglion cells (ipRGCs) respond to light directly through melanopsin, and indirectly due to signals originating from absorption of light by the other four pigments.<sup>30–35</sup> Thus ipRGCs combine the photic signals in the non-visual system, signals which can either entrain or disrupt the circadian timing of genetic expression in the suprachiasmatic nuclei (SCN), which in turn regulate numerous peripheral circadian rhythms, to be found in almost all cell types. Downstream effects may depend on stimulation of just melanopsin or of any combination of the five photopigments, so light weighted for all five photopigment sensitivities should be measured (see Figure 1) and reported, to unravel the contribution of each photoreceptor type in determining nonvisual responses in the brain and body.<sup>35</sup>

#### Light exposure measurement

When measuring light exposures in occupational health studies, it is necessary to consider light level, spectrum, timing and duration of exposure and the exposure history of the participant, <sup>36</sup> preferably captured with personal dosimeters (or actigraphs) as well as *in situ* lighting measurements. Until recently, almost all field studies and many laboratory studies reported only sample measurements of illuminance and correlated colour temperature (CCT)<sup>7,37,38</sup> or compared a

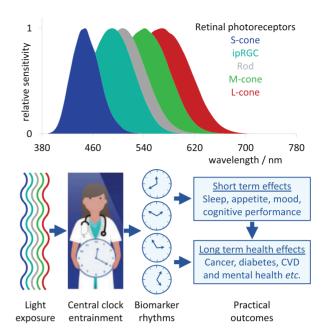


Figure 1. Non-visual effects of light on circadian regulation and long-term health. Top: the non-visual system comprises five different photo-receptor-based spectral sensitivities. Bottom: ipRGCs combine photic information from these five channels to drive entrainment of the central clock in the SCN. Clock signals provide circadian information to entrain downstream responses, in anticipation of daily exogenous and endogenous demands, which also act as biomarkers of subjective physiological timing. Important biomarker rhythms include plasma melatonin, cortisol and core body temperature. Short term responses, including sleep, appetite, mood and cognitive performance are highly non-linear: work and sleep schedules and social factors can also influence or disrupt these rhythms.

particular type of lamp or CCT versus another, <sup>7,11</sup> or indirect versus direct lighting, <sup>39</sup> without determining actual light exposures. Relying on metrics based on human brightness perception and colour vision (i.e. photometry and colorimetry) for describing experimental light conditions is now strongly discouraged, <sup>40</sup> because they do not reflect non-visual effects of light.

Spectroradiometry would provide the ideal information, but spectrometers are bulky, especially compared with actigraphs incorporating light sensors. At present, the optical performance of such wearables is highly variable, and none of them effectively measures more than two of the five spectral channels recommended for research on nonvisual effects of light, 41–45 demanding careful selection and prior characterization of light dosimeters. Advances in technology may improve this situation in the future.

#### Shift work and light exposure metrics

Shift work characteristics including timing of shifts, shift rotation and on-off rostering all have implications for LAN and daytime light exposures that may cause regular circadian disruption. It has been recommended that the duration, timing and intensity of light exposure at work plus number of years worked, shift pattern and rotation should be included in the description of shift work in epidemiological studies. However, the characteristics of light exposure including LAN that may predict different health aspects are still unclear. It has also been suggested that studies include data on exposures both at work and outside working hours. The NoVEL network participants reflect an increasing number of study groups that are conducting field research in which daylight levels and light exposure information are collected continuously over 24 h each day.

To date, only a limited number of metrics directly based on the features of the non-visual system have been proposed which offer insights for circadian lighting design. The most cited metrics are 'Circadian Stimulus – CS', <sup>47–49</sup> and melanopic irradiance, with or without temporal smoothing. <sup>35,50,51</sup> These metrics are not fully developed, and determining the best approach will require further dedicated research data, in both the field and the laboratory. Future exposure metrics could differ with regard to different shift types or shift rotation patterns. For example, workplace light exposure data of daytime office work may include more information on sunlight exposure, including ultraviolet radiation (UVR) for vitamin D synthesis, and be concerned less with LAN.

#### Translational field studies

Controlled laboratory studies enable monitoring of the participants, to support them in achieving higher levels of compliance. Whereas they can simulate broad-brush aspects of work, findings obtained in laboratory settings may not always be readily generalizable, as it is difficult to introduce the same level of control over conditions in real work environments, especially for shift work.

Although field studies lack the same level of control of the environment, they provide—in contrast to laboratory work—valuable information on improving real life working conditions. Participants in field studies are exposed to individual variables such as personal habits (e.g. the quantity of sleep and commuting). They follow everyday routines (e.g. housekeeping, preparing food, taking care of children and pets). Group level variables may include socioeconomic links to light pollution (living in the city), cultural aspects (e.g. as reflected in architecture), season, latitude etc. Such uncontrollable exposures and complex behaviours are part of everyone's lives, as well as being unavoidable aspects of working out of phase with the light cycle. This inherent unpredictability should always be taken into account when estimating the effectiveness of interventions in real-life settings.

#### Circadian biomarkers

Measurement of circadian rhythms requires the use of biomarkers. Salivary cortisol provides a good indication of plasma levels, <sup>52</sup> whereas a recent study questioned whether the same is true of salivary melatonin, <sup>53</sup> possibly due to additional melatonin produced in the salivary glands. Alternatively, field researchers looking for more reliable data on nocturnal melatonin amplitude might consider analysis of urine samples. <sup>54</sup>

Participants in field studies of workers are primarily healthy adults, for whom the variations in biomarkers can be relatively small.<sup>55</sup> Hence it is crucial to use precise and sensitive methods under analytical control, based on biomarkers that are stable during handling and shipping.<sup>56</sup>

# Cognitive performance testing and ecological momentary assessment (EMA)

To capture feelings, thoughts and behaviour as they evolve during a real-life intervention trial, ecological momentary assessment (EMA; or experience sampling methodology) can be used.<sup>57</sup> EMA has several advantages to using questionnaires before and after a trial, including greater ecological validity with minimal retrospective bias. The frequency of assessments provides higher sensitivity to intervention effects and data concerning patterns in daily life.<sup>58</sup>

EMA is well suited to assess the non-visual effects of light on mental health, such as mood disorders. The effects of exposure conditions and disruption of the circadian rhythm on cognition processes, such as processing speed, alertness, attentional control, inhibition, planning and, short-term and working memory, should also be considered. Associations linking both social interaction and mood to changing light exposure have been shown using EMA coupled with a wearable light dosimeter. EMA methodology may be integrated within interventions, often referred to as EMA/I, where feedback or advice is presented based on an individual's responses to the EMA questions.

#### Summary

The impact of light exposures on the health and well-being of shift workers and indoor daytime workers has not been explored in sufficient detail. Advice to promote positive health outcomes for these groups should be based on evidence taken from, or validated by, well-designed field studies into the effects of light exposure. These effects are not just driven by artificial lighting in the workplace, but may depend on exposures to daylight and the influence working hours have on 24-h exposures and workers' lifestyles.

To obtain the best foundation for future health advice on optimal light conditions at work and light exposures on working days, there is a need to develop better field studies on circadian rhythms and other non-visual effects of light, combining diverse techniques and areas of expertise, including:

- experimental designs to unravel causality for long-term health outcomes, including detailed descriptions of shift characteristics;
- accurate personal light exposure measurements of the five recommended spectrally-weighted channels, to reveal the aspects of light ultimately affecting health;
- robust validated biomarkers to measure diurnal rhythms, and high-quality cognitive performance techniques, including interviews concerning chronometry and organizational aspects of the workplace; and
- EMA to monitor changes in behaviour and well-being on an ultradian scale, together with input from participants and wider stakeholders, which inform the deployment of individualized and appropriately timed interventions.

To effectively tackle the occupational and public health challenges of light exposure, particularly in shift work, we call for a greater use of tailored multidisciplinary prospective approaches with sufficient follow-up to address long-term consequences of lifestyle-like interventional changes.

Conflict of interest: None declared.

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