

D3.7 REPORT ON METRIC TO QUANTIFY BIOLOGICAL LIGHT EXPOSURE DOSES

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AUTHOR:

Marina Giménez, RUG

CO-AUTHORS:

Luc Schlangen and Dieter Lang, LE
Domien Beersma, RUG
Philipp Novotny and Herbert Plischke, MUAS
Katharina Wulff and Matthäus Linek, UOXF
Christian Cajochen, Jakob Löffler
Ruta Lasauskaite UNIBAS/UPK
and Pramod Bhusal and Liisa Halonen, AALTO

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EXECUTIVE SUMMARY

Light is necessary for vision, but it is also influencing our mood, alertness, attention and the body's internal biological clock, which helps us to wake up in the morning and fall asleep in the evening. These latter functions of light are called non-image forming (NIF) effects of light.

Different light conditions (e.g. intensity, color, exposure, time of day) have different effects on humans. We know that the human eye is sensing the different colors (blue, green, red) via different photoreceptors, which are sensitive to different wavelength ranges. By designing lighting installations that consider all wavelengths and corresponding photoreceptor inputs, we can give people the light that makes them feel well and stay healthy.

This report explores how to assess and quantify light conditions for their ability to produce non-image forming effects. With other words, we wanted to know, which kind of light has what kind effect on people, and what metrics could describe that light.

We found via a meta-analysis of scientific reports, that the currently used lux (photopic irradiance) is not the most appropriate unit to describe how much light is needed to generate the biological (NIF) effects of light. Lux is characterizing light only with respect to vision, not with respect to its biological NIF effects. In contrast to this, α -opic irradiances and the melanopic daylight equivalent illuminance are useful metrics to support light designers to decide, which light conditions can be used to promote, or avoid, certain biological (NIF) responses. These metrics are expected to be particularly effective, when designing light conditions with narrow spectral bands or different color temperatures.

Healthy interior lighting requires dynamic lighting designs in which the melanopic irradiance (or melanopic daylight equivalent illuminance) is high during daytime, especially in the morning, while it should be low during the last 2 hours before bedtime and at night.

SUMMARY

This report explores how to assess and quantify light conditions for their ability to produce biological, non-image forming (NIF) effects. Well known NIF effects are the acute influence of light on mood, alertness and attention, as well as the critical role of light in the regulation of our body clock, sleep/wake pattern, and their 24 hour (circadian) rhythmicity. Based on data selected from a literature overview of different NIF responses to light, we explored whether photoreceptor weighted irradiances can be used as a metric to compare the various light conditions between the studies. Dose-response curves for four different NIF responses were made: subjective sleepiness, melatonin suppression, performance on a visual concentration task (d2) and depression scores. These responses were chosen because of their particular relevance for our living environment in the public and domestic domain, as encountered in workplaces, schools, hospitals, and (elderly) care homes.

Despite the variability of the data included in the meta-analysis in this report the following preliminary conclusions can be drawn:

- All five kinds of photoreceptors (rods, blue-cones, green-cones, red-cones, and melanopsin containing ganglion cells) of the human eye can contribute to NIF effects of light. Each photoreceptor input can be characterized by its corresponding alpha (α)-opic irradiance, where α denotes the kind of photoreceptor.
- The standard white light conditions as used in many scientific studies are inappropriate to decide which quantity from the five alpha-opic and photopic irradiances is predictive for the light conditions ability to achieve NIF responses. For white light all these irradiances increase approximately linearly with the light intensity.
- So far the α -opic irradiances do not add much to discriminate between commonly used standard white light conditions. They are expected to be more useful predictors for NIF effects in more extreme light conditions (dim light, very low/high color temperature, or narrow band light)
- Some NIF effects, like subjective alertness and the nocturnal suppression of the sleep-supporting hormone melatonin, seem to correlate more strongly with the melanopic irradiance (or melanopic lux) than with the photopic irradiance (expressed in lux). This is more enhanced when only considering those studies that use light with narrow spectral bands. The melatonin data (best quality and range of conditions) shows the impact of spectral distribution of light in which photopic lux fails to describe the response effectively.
- It is recommended to start using α -opic irradiances and melanopic daylight equivalent illuminances as a metric to decide which light conditions can be used to promote, or avoid, certain NIF responses. The metric is expected to be particularly effective when designing light conditions with narrow spectral bands or different color temperatures.
- Healthy interior lighting requires dynamic indoor lighting designs that provide a high melanopic irradiance (or melanopic daylight equivalent illuminance) during daytime, especially in the morning. During the last 2 hours before bedtime and at night, the light intensity (lux) and melanopic irradiance should be sufficiently dimmed to facilitate good sleep. With these inclusions, dynamic lighting strategies are a powerful tool to prevent sleep and body clock disturbances.

The content of this report will be used for a submission to the Journal of Lighting Research and Technology. In that publication a definitive position on SI compliant units for photoreceptor weighted light intensities will be provided.

INTRODUCTION

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1 | INTRODUCTION

Light is a major environmental factor playing a role in human health and well-being. On a daily basis, light intensity and spectral composition both change throughout the day from dawn to dusk and represent the strongest environmental cue to set the phase of our biological clock.

Light synchronizes physiological and psychological rhythms to the 24-hour rhythm of the environment (Pittendrigh 1960). Light has also acute alerting and activating effects (Cajochen 2007), can affect mood (Wirz-Justice 2007), and, when applied at night, suppresses melatonin production (Lewy et al, 1980). These are some examples of the so-called non-image forming (NIF) effects of light in humans.

The NIF effects are initiated by a phenomenon known as retinal photoreception, altering the state of the retinal photopigments, ultimately evoking physiological responses. Retinal photoreceptors comprise three main types; the rods, the cones and the melanopsin containing photosensitive retinal ganglion cells (pRGCs). Concerning cones three different types can be distinguished; blue-cones, green-cones and red-cones. The photoreceptors differ from each other in their spectral sensitivity to light and in their stimulation efficiency, as they contain different photopigments¹.

In this sense, the spectral composition, intensity, timing and dynamics of light are key characteristics that will determine the final response. This critical information needs to be taken into account when quantifying NIF responses to light exposure; different NIF responses can result from light sources of similar irradiance but different spectral composition.

It is relevant to note that the sensitivity of the NIF system is shifted towards the short wavelengths of the light spectrum (Brainard et al, 2001; Thapan et al, 2001) as compared to the visual system. This is due to the melanopsin photopigment (Provencio et al, 2000, 1997) in the pRGCs which plays an important role, assisted herein by rods and cones, in transferring light information to the NIF system. The melanopsin within the pRGCs is activated by short wavelength light with an absorption peak at about 480 nm (Berson et al, 2002; Hattar et al, 2002; Provencio et al, 1997). In line with this, recent studies have shown that melanopic (equivalent) lux is more accurate at predicting NIF responses in mice as compared to the standard photopic lux unit (Al Enezi et al, 2011; Brown et al, 2013). Similar conclusions were drawn for maximal changes in subjective sleepiness scores in response to light in humans (Hommes and Giménez 2015).

This clearly underlines that next to the image forming system (photopic lux) it is important to implement a light unit measure that takes into account the aspects of the NIF system. The spectral luminous efficiency function $V(\lambda)$ is the standardized sensitivity of the human eye for photopic vision. $V(\lambda)$ is based on the sensitivity of the cones in the human eye. $V(\lambda)$ has been used since 1924 after publication by CIE and has been republished by CIE as standard CIE 18.2 in 1983, as CIE S 10E in 2004 and by ISO as ISO 23539 in 2005. For scotopic vision at a low adaptation luminance the $V'(\lambda)$ function is used (see also CIE S10E), which describes the sensitivity of the rods in the human eye.

¹ Rods: peak sensitivity: ~500 nm, photopigment: rod opsin;
blue-cones, also called S (short wavelength sensitive) cones: peak sensitivity: ~420 nm, photopigment: cyanolabe;
green-cones, also called M cones: peak sensitivity: ~535 nm, photopigment: chlorolabe; red-cones, also called L cones: peak sensitivity: ~565 nm,
photopigment: erythrolabe;
pRGCs: peak sensitivity: ~480 nm, photopigment: melanopsin.

Recommendations are urgently needed for a metric that not only considers rod and cones but also takes the melanopsin photoreceptor into account. A first attempt to achieve this goal was taken by Lucas and colleagues (Lucas et al, 2014).

They published a weighting function (action spectrum) for the melanopsin containing pRGC receptor and developed a tool to measure light using photoreceptors' sensitivity-weighted irradiances given an output for all photoreceptors (for which they suggested the unit α -opic lux, where α stands for one of the five known photoreceptors) next to the photopic lux. Despite publishing a revised version in 2015 which avoids the unit "melanopic lux" and other " α -opic lux" and is only giving irradiance data in energy-unit W/m^2 , the first version and the unit "melanopic lux" has found wide acceptance among scientists and is continued to be used (see also the discussion section).

Using photoreceptor weighted irradiances as light unit next to the standard photopic lux, we set out to create dose-response curves for different NIF responses: subjective sleepiness, melatonin suppression, performance on a visual concentration task (d2) and depression scores. These responses are of particular relevance for public and domestic settings like, workplaces, schools, hospitals, and (elderly) care homes. It is a step in generating a tool to help assess the magnitude of different NIF responses that may be expected for a given light exposure or lighting condition.

Unfortunately, the studies included in the present work are not all equally informative and are mostly based on white light exposure. Nonetheless, we aimed at providing a tool that can be further developed, tested and be used for hypothesis generation. Moreover, using photoreceptors weighted irradiances allows for comparison between the different studies and the generation of an overview for the different NIF responses.

These application domains together with smart cities are central to WP3 of the SSL-erate project. Unfortunately, there is very limited research carried out on outdoor environment with regard to NIF responses. Some of the existing studies either fail to report a description of the lighting used (intensity, spectra, etc.) or fail to provide the quantified results. Therefore, current research evidence in outdoor lighting is not sufficient to develop dose relationship in relation to well-being and other biological effects. Even if the current understanding is that the moderate and low levels of outdoor lighting are not sufficient to significantly stimulate pRGCs (e.g. to elicit melatonin suppression), the contributing role of cones and rods to non-visual effects at low light levels has been reported (Zeitzer et al. 1997, Chellappa et al. 2010) but the effects are not sufficiently understood yet. There is a need of further studies investigating and measuring well-being effects of outdoor illumination on humans.

METHODS

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2 | METHODS

2.1 Quantification of photoreceptor weighted irradiances

A macro-based Excel worksheet, called “HCL Toolkit”, has been created by Dieter Lang and provided to the SSL-erate consortium which allows to calculate α -opic lux data according to Lucas et al. (2014) for a large number of different light sources with various color temperature and spectral characteristics. In addition the Excel worksheet is providing α -opic irradiance data as described in the “CIE_784_TN003_Toolbox” developed by Lucas and colleagues (Lucas et al, 2014).

Another way to quantify to what extent a light condition stimulates each of the five (α -opic) photoreceptors is to express the amount of daylight illuminance that would be needed to produce a similar stimulation of the α -opic channel. Hereto the concept of α -opic daylight equivalent illuminance is introduced. This new output is included in the “HCL Toolkit”. The α -opic daylight equivalent illuminance $E_{V,\alpha,S}$ of a given light exposure S , is equal to the illuminance $E_{V,D65}$ that would be needed when a light source with spectral characteristics equivalent to standard illuminant D65 (natural daylight at 6500 K) is used to produce an α -opic irradiance $E_{e,\alpha,D65}$ that equals the α -opic irradiance $E_{e,\alpha,S}$ of S (see Figure 1).

As such, the quantity $E_{V,\alpha,S}$ is equivalent to the amount of daylight that is roughly needed to achieve the same α -opic irradiance as the current light condition.

For daylight D65 the α -opic daylight equivalent illuminance is by definition equal to the photopic illuminance expressed in lx. For the case that α denotes the melanopsin receptor, the value of the melanopic daylight equivalent illuminance, measured in lx, for any arbitrary light source, is equal to the value of the “melanopic lux”, according to Lucas et al., 2014, multiplied by the melanopic action factor for D65 of 0.906 which denotes the ratio of the melanopic weighted spectral power distribution to the photopic weighted spectral power distribution of a D65 light source.

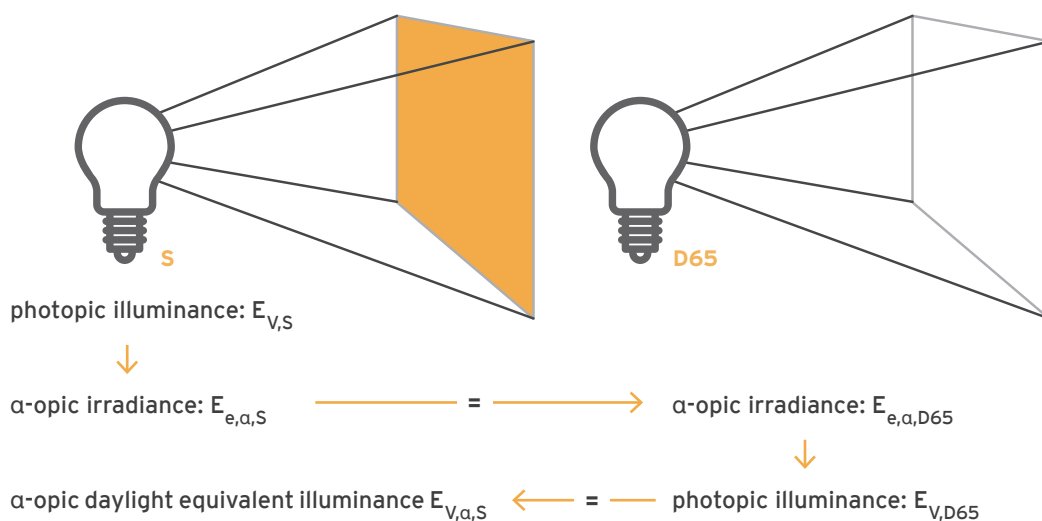


Figure 1 - Concept of α -opic daylight equivalent illuminance.

The functionality of the worksheet allows conversion of any photometric light input data to the photoreceptor-relevant input data for the 5 different types of photoreceptors.

2.2 Selection of studies

The NIF responses included in the present work are:

- subjective sleepiness assessed by the Karolinska Sleepiness Scale (KSS),
- endogenous melatonin levels (i.e. degree of suppression by light),
- concentration performance assessed by d2-test,
- depression scores assessed by different rating scale (see methods section).

A search on the electronic database PubMed (with the greatest inclusion search beginning in 1966 until April 2015) was conducted with keywords including the different NIF responses and words like: light, circadian, human, illuminance.

In general, only studies that contained a full description of the light characteristics were included. Namely, information on (1) level of illuminance, (2) colour temperature (3), lighting type, (4) spectral peak and width of monochromatic LEDs if LEDs were used, (5) duration and (6) time-of-day of light exposure had to be present in the publication. Absolute outputs of the different NIF responses have been derived either from figures or from tables/text.

Further, some specific criteria had to be met for the different NIF responses.

For KSS only those studies reporting on acute effects (thus, not for instance weekly averages) within 2 hours of the light exposure were included. If daytime sleep was part of the study design and KSS was measured on the preceding evening/night, the study was not included. We did not distinguish between papers that investigated the effects of light on KSS during daytime and evening time. We assumed that the acute alerting effects of light are similar at different circadian times (Ruger et al, 2005), although this assumptions needs to be confirmed by further studies.

For melatonin suppression, only studies that measured melatonin either in saliva or plasma were included. The light exposure had to occur during the biological evening or night (i.e., the start of the light exposure had to be between 19:00 and 02:30 h) with exposure duration of at least 30 minutes. Further, the study design should include a dim light condition or a pre-dark adaptation period. Studies reporting on d2-test outputs were excluded from analysis when the studies did not provide sufficient data.

With regard to depression scores, each study had to report baseline values, time of day and length of daily light treatment exposure as well as total duration of the treatment and the age of the participants (only studies with patients older than 18 years were included). When studies contained a combination of treatments, e.g. sleep restriction, exercise and light therapy, and additional outcome measures (e.g. binge eating, mental performance, sleep quality), only light treatment and its effects on depression were included in the analyses.

In total, 57 studies have been included, with 11 studies for subjective sleepiness (KSS), 27 studies for melatonin suppression, 6 for concentration performance (d2-test) and 13 for depression scores. The light characteristics of the analyzed studies are given in the Appendix.

2.3 Output from selected studies

The following outputs are reported:

1. Absolute KSS scores 60 and 120 minutes after lights on.
2. Percentage of melatonin suppression.
3. Given the large learning effect over time in d2-test performance, gain scores (i.e. difference between post- and pretest scores) were calculated as proposed by Keis et al. (2014) instead of absolute values (Keis, Helbig, Streb, & Hille, 2014). Gain scores from the intervention group were subtracted from those in the control group to assess the effects of light. Results are expressed as percentage. Outputs reported are “fewer errors” and “concentration performance”. Since most of the available data on d2-test vary in control or pre-illumination conditions, comparison is difficult. In order to bypass this problem we have chosen to plot the data against -opic lux; the difference in light intensity per opsin that leads to a certain output score.
4. Depressions scores covered a range of depression scales including two types of Hamilton Depression Rating Scales (HDRS, 17 items; SIGH-SAD, 21 items of the HDRS plus 8 of the atypical item subscale), Beck Depression Inventory (BDI, 21 items), Major Depression Inventory (MDI, 12 items), Edinburgh Postnatal Depression Scale (EPDS, 10 items) and the Geriatric Depression Scale (GDS, 30 items). Therefore, scores had to be scaled to enable each outcome score to be adjusted relative to the other questionnaires' scores. The dose response curve was defined as the product of illuminance (E) and the treatment exposure time (tT), where the exposure time was derived from the product of daily exposure duration (tE) and treatment duration (nT). See equation 1.

$$D = E \cdot t_T = E \cdot t_E \cdot n_T \quad (\text{eq. 1})$$

$$[D] = lx \cdot h \cdot 1 = lxh$$

2.4 Statistics

All outcomes measures were plotted against light intensity. Light intensity was reported as cyanopic, melanopic, rhodopic, chloropic and erythropic lux, as defined in Lucas et al. (2014) as well as against photopic lux.

Given the intrinsic nature of the different NIF responses, different approaches had to be taken. KSS, d2-test and depression scores showed a linear relationship with light intensity. Pearson correlations were used to assess the strength of correlation between KSS and light intensity and between d2-test performance and light intensity.

The relationship between depression scores and light intensity was assessed by means of the Spearman's correlation test.

Melatonin suppression showed a sigmoidal relationship between relative melatonin suppression and light intensity. A four parameter logistic model (equation 2) has been fitted to the data, since four parameter logistic models estimate well responses that have a sigmoidal relationship with increasing stimulus strength. Correlation coefficients, R², and p values are reported.

$$y = y_0 + a / (1 + \exp(-(x - x_0)/b)) \quad (\text{eq. 2})$$

RESULTS

3 |

3 | RESULTS

The relationship between the NIF responses and the α -opic lux as well as for the photopic lux is shown in the Figures 1 to 6. Outputs of the different correlations (i.e. correlation coefficients, R², and p values) for each NIF response are shown in Table 1.

Table 1 - Correlation numbers for KSS, d2-test and depression ratings as well as fit parameter of the logistic model for melatonin suppression.

		Pearson correlation				Logistic model
			correlation coefficient	R ²	p value for correlation	r ²
KSS	60' ALO	Photopic	-0,49	0,26	0,005	
		Cyanopic	-0,52	0,32	0,002	
		Melanopic	-0,62	0,38	0,0003	
		Rhodopic	-0,47	0,25	0,005	
		Chloropic	-0,48	0,26	0,005	
		Erythropic	-0,49	0,27	0,004	
	120' ALO	Photopic	-0,48	0,23	0,02	
		Cyanopic	-0,55	0,3	0,008	
		Melanopic	-0,6	0,35	0,004	
		Rhodopic	-0,57	0,32	0,006	
		Chloropic	-0,54	0,29	0,01	
		Erythropic	-0,52	0,26	0,02	
Melatonin	total suppression	Photopic				no fit
		Cyanopic				0,41
		Melanopic				0,76
		Rhodopic				0,73
		Chloropic				no fit
		Erythropic				no fit
d2 test	% concentration performance	Photopic	0,88	0,78	0,2	
		Cyanopic	0,85	0,73	0,02	
		Melanopic	0,85	0,78	0,03	
		Rhodopic	0,86	0,76	0,03	
		Chloropic	0,87	0,72	0,02	
		Erythropic	0,88	0,74	0,2	
	% less errors	Photopic	0,23	0,05	0,56	
		Cyanopic	0,27	0,07	0,48	
		Melanopic	0,27	0,05	0,49	
		Rhodopic	0,26	0,06	0,50	
		Chloropic	0,24	0,07	0,53	
		Erythropic	0,22	0,07	0,57	
Depression Rating	Relative Scaled Score		Sperman's rho correlation		p from rho	
		Photopic	-0,816	0,59	0,01	
		Cyanopic	-0,778	0,59	0,01	
		Melanopic	-0,823	0,59	0,01	
		Rhodopic	-0,824	0,59	0,01	
		Chloropic	-0,701	0,59	0,01	
		Erythropic	-0,813	0,59	0,01	

With regard to KSS, a linear relationship with the logarithm of light intensity was found, both 60 and 120 minutes after lights on (Figure 1).

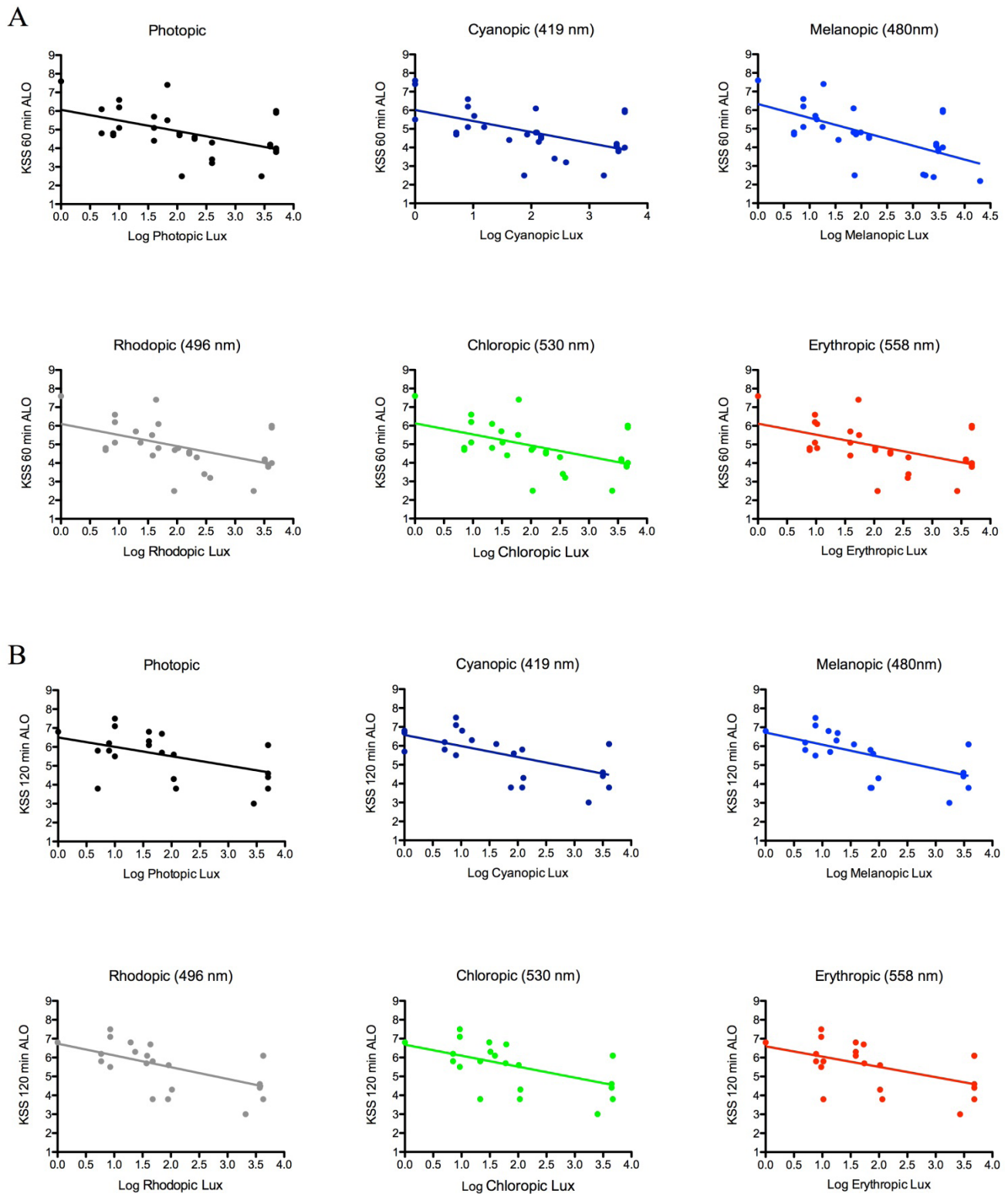


Figure 1 - KSS dose response curves. KSS outputs against each α -opic - and photopic - lux after A) 60 minutes and B) 120 minutes of light exposure. The line illustrates the (Pearson) correlation. All correlations were shown to be significant.

Photopic lux as well as all α -opic lux revealed a significant correlation with slightly higher coefficients for the melanopic lux (see Table 1).

With regard to melatonin suppression, a sigmoidal relationship with increasing stimulus strength was found (see Figure 2).

Only cyanopic, melanopic and rhodopic lux could be fitted successfully to a four parameter logistic model with best fits for melanopic- and rhodopic-lux. The other opsins showed no significant correlation (see Table 1).

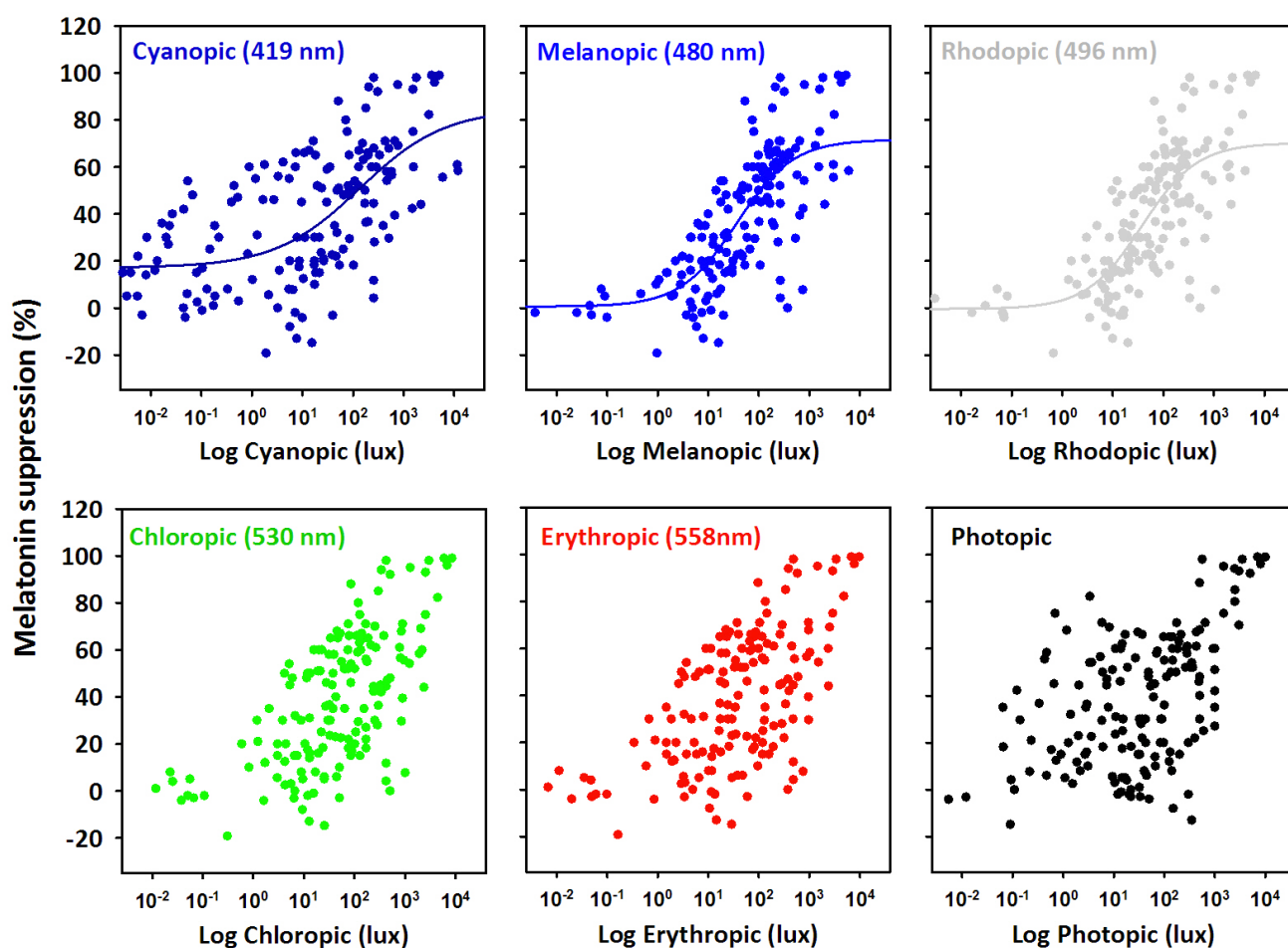


Figure 2 - Melatonin suppression dose-responses curves. Total melatonin suppression outputs against each α -opic and photopic lux. The line shows the fit to a logistic model. A significant fit was only observed for cyanopic, melanopic and rhodopic lux.

With regard to the d2-test outputs, only percentage of concentration performance showed a significant correlation with light intensity for all α -opic and photopic lux.

The observed linear relationships are shown in Figure 3. Statistically significant correlations were found for all α -opic lux (see Table 1).

However, for the percentage of fewer errors (Figure 4), no significant correlations were found for the opsins (see Table 1).

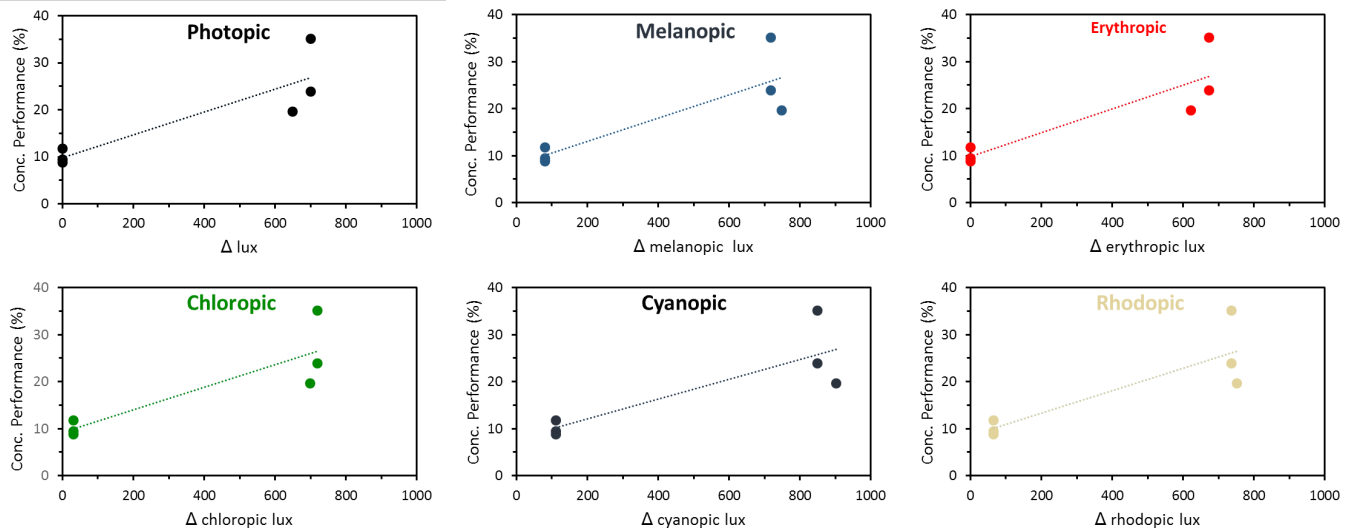


Figure 3 - Concentration performance (d2-test) dose response curves. Concentration performance (%) outputs against the changes in each α -opic and photopic lux. The line shows the (Pearson) correlation. All correlations were found to be significant.

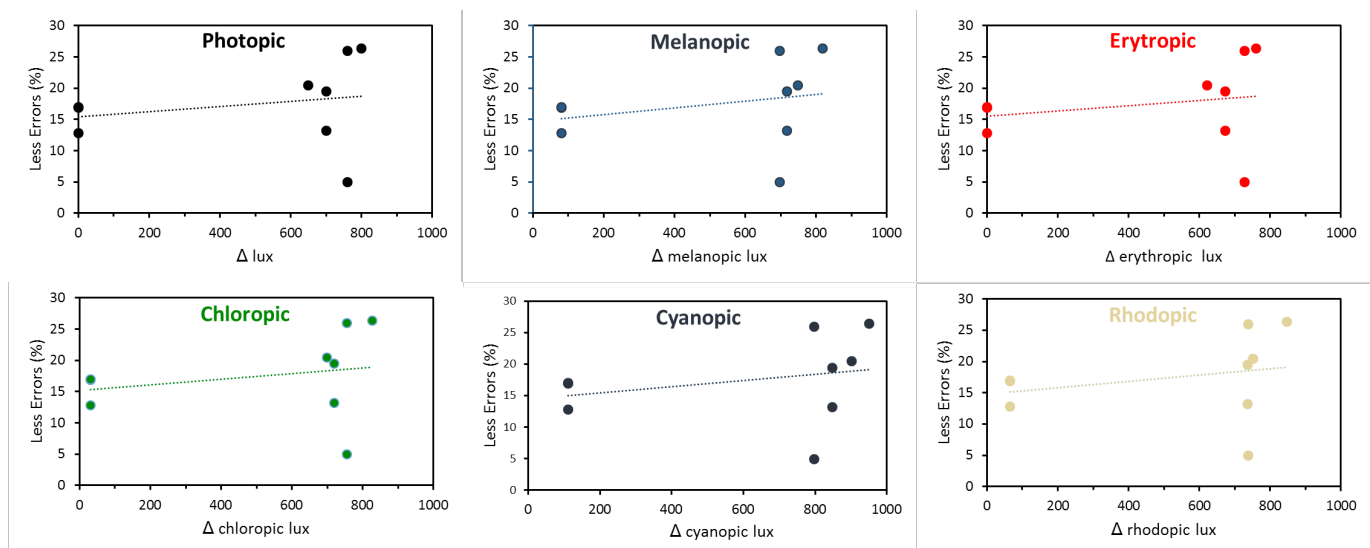


Figure 4 - Less errors (d2-test) dose response curves. Less errors (%) outputs against the changes in each α -opic and photopic lux. The line shows the (Pearson) correlation. None of the correlations was found to be significant.

With regard to the depression outcome, depression scores decreased in a dose-dependent manner in all 13 studies (colour-coded) for all α -opic and photopic lux (see Figure 5).

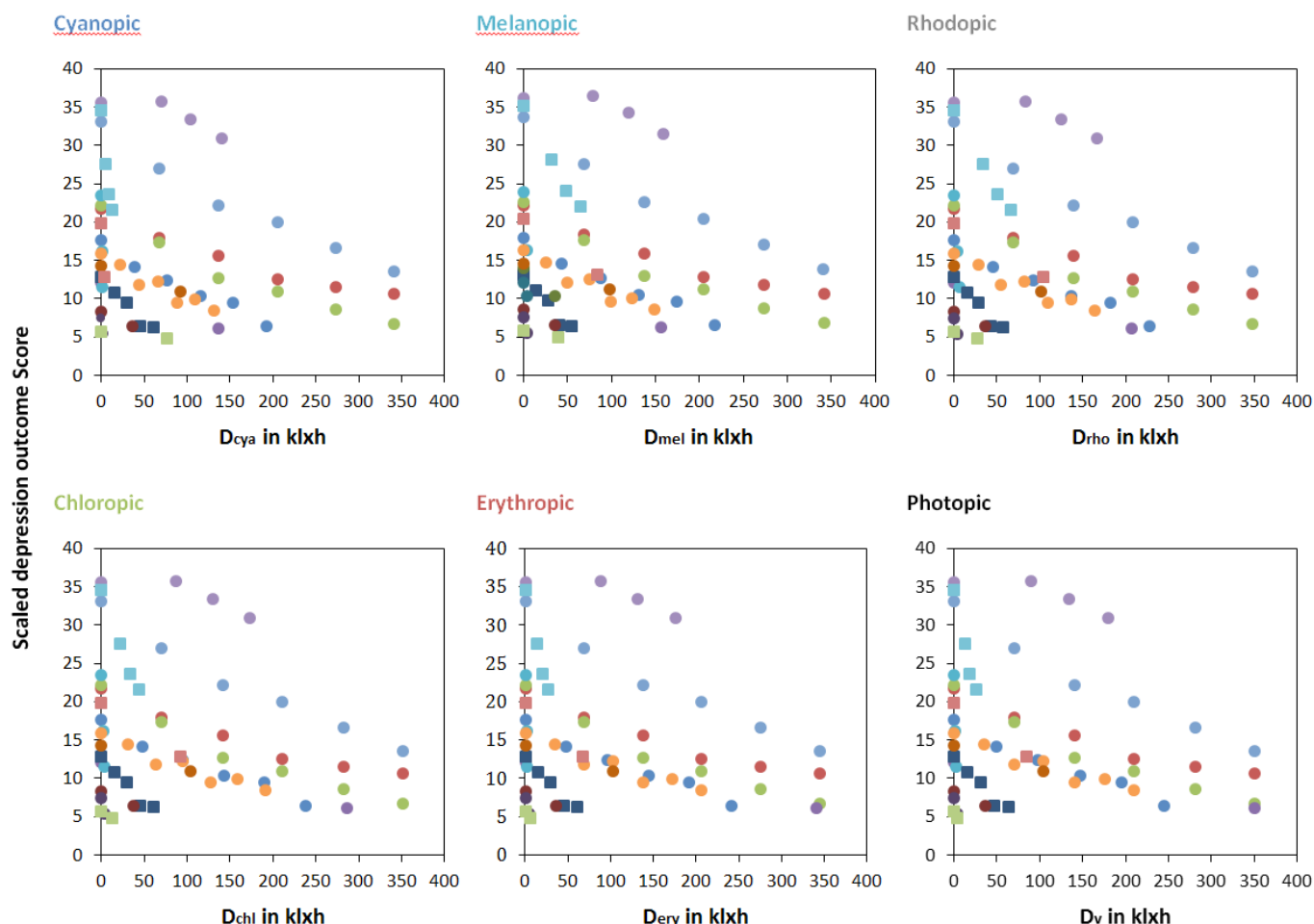


Figure 5 - Scaled depression scores dose response curves. Scaled depression outcome Scores, calculated for treatment conditions across all studies against all α -opic and photopic lux. Light dose given in kilolux hours (D in klxh). Each colour represents a specific study. Values along the vertical y-axis at zero dose represent the scaled outcome scores at baseline.

Scaled outcome scores made comparison between different scales and studies possible. Dose-dependent decrease in scaled depression scores is notable in all treatment groups. Circles indicate fluorescent light sources; squares indicate LEDs light sources.

Given the wide range of baseline scores (baseline matches dose zero), the Scaled depression Score values were normalized with respect to the baseline measurement (baseline scores set at 100%, Figure 6). A monotonic decrease in depression with increasing light dose regardless of clinical condition can then be observed for all α -opic and photopic lux (see Table 1 and Figure 6).

LED-type light sources (squares, 5 studies) needed much lower doses to achieve the same reduction in depression as fluorescent-type light sources (circles, 8 studies) but their slopes were not significantly steeper (Mann-Whitney test: $p=0.44$).

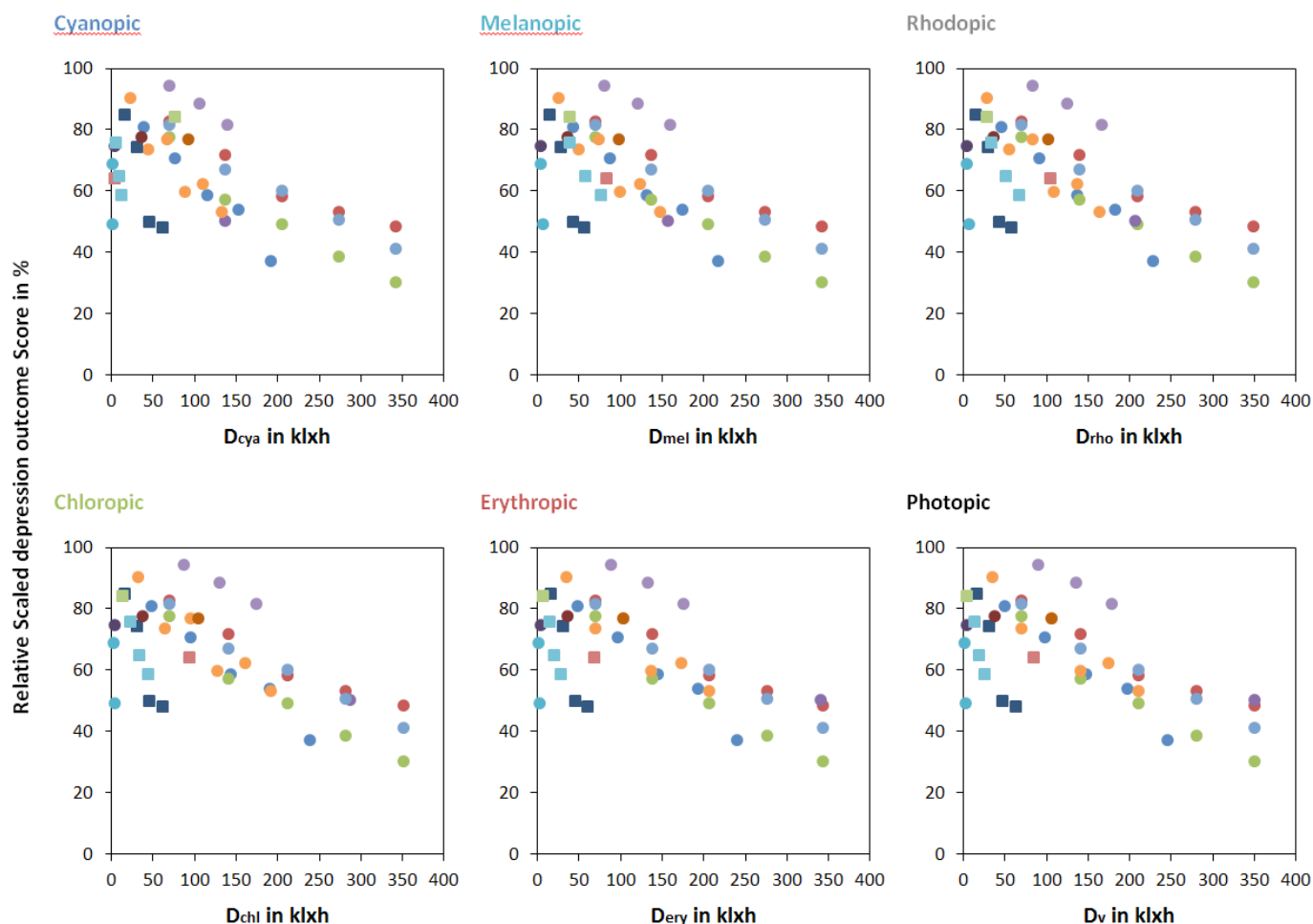


Figure 6 - Relative scaled depression scores dose-response curves. Relative scaled depression scores outcome against all α -opic and photopic lux. Outcome scores are shown as relative to their baseline scores being 100 %.

Depression scores decrease in a dose-dependent manner shown proportionally across all treatment groups. Light dose given in kilolux hours (D in klxh). Each colour represents a specific study. Circles indicate fluorescent light sources; squares indicate LEDs light sources.

Not all studies showed a difference of light treatment on depression in comparison to the placebo condition (Table 2). Since placebo conditions are debatable for light treatment studies, we were more interested in the effect magnitude over time across the treatment period of all studies. The effectiveness was greatest within the first two weeks of treatment and then plateaued out on a lower level, indicating that individual depression scores have decreased to near-remission levels in several studies (see Figure 7).

Table 2: Statistical result listed for light therapy studies.	
Study	Original Statistical result p-values
Wirz-Justice et al. 2011	<0.01
Martiny et al. 2009	<0.01*
GOEL et al. 2005	<0.05
Benedetti et al. 2003	<0.05
Corral et al. 2007	<0.001
Youngstedt et al. 2011	n.s.
Paus et al. 2007	<0.05
Braun et al. 1999	n.s.
Martiny et al. 2005	n.s.
Lee et al. 2013	<0.05
Royer et al. 2012	n.s.
Loving et al. 2005a	n.s.
Loving et al. 2005b	n.s.

* only significant for low cortisol awakening response

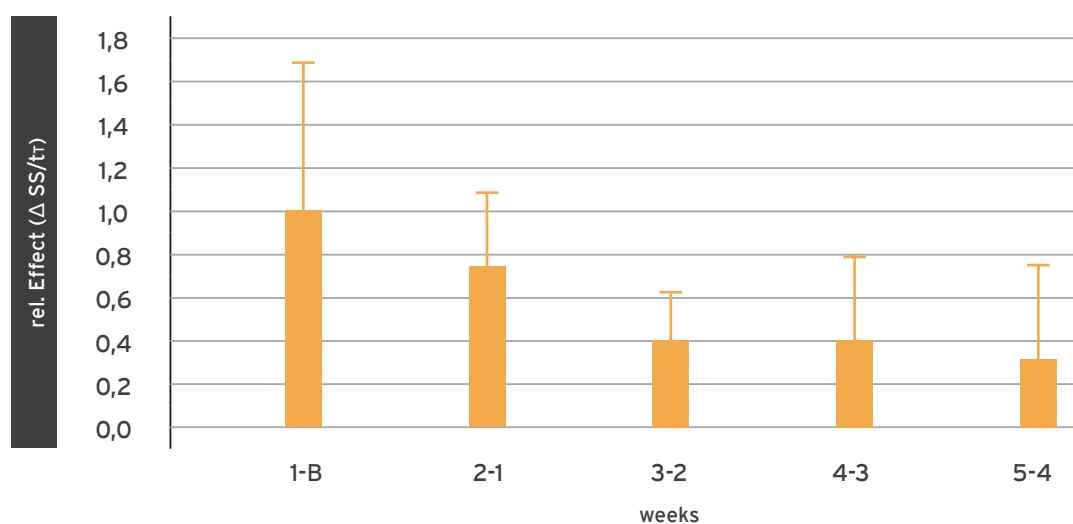


Figure 7 - Effectiveness of the light intervention using depression rating scores from week-to-week. B: baseline. ΔSS : Change in the scaled depression outcome score. tT: treatment time.

DISCUSSION

4 | DISCUSSION

The present work comprises a meta-analysis of the currently existing literature about the NIF effects of different light conditions on subjective sleepiness (KSS), melatonin suppression, cognitive performance (d2-test) and depression scores.

We have constructed dose-relationships between each outcome variable and light intensity by plotting the NIF responses against the standardized light unit lux (i.e. photopic lux), as well as against the different α -opic lux as described by Lucas and coauthors (Lucas et al, 2014). Our aim was to provide evidence for the dialog on whether using new metrics of light instead of the standard photopic lux, can better explain the effects of light on the broad range of NIF responses in humans.

The overview generated for the different NIF outputs allows visualizing different ranges of light intensity at which a certain response can be expected.

Thus, this represents a potential step towards defining recommendations for light specifications. However, given the nature of the present work (a compilation of existing data) recommendations should be made with care and certainly within the limit of light ranges used in the different studies. Moreover, the ultimate response will depend on the time of the day at which exposure occurs (Khalsa et al, 2003), as well as internal timing (Roennenberg et al, 2007).

The response can be further sensitize or be reduced depending on previous exposure to darkness (Smith et al, 2004) or light (Hérbert et al, 2002), respectively.

These aspects have to a large extent been disregarded in the analysis so far. In general, all NIF responses assessed in this review showed a favourable dose response with light intensity. The only response that failed to show a significant correlation with light dose, though going into the expected direction, was the percentage of fewer errors in the d2 performance task. Already by small changes in α -opic lux a relatively large response is observed and larger changes in α -opic lux do not seem to add more to the response.

With regards to the metrics (i.e. whether we could benefit from photoreceptors weighted irradiances), the main obstacle we encountered was that most studies used in the present work have used white light sources. Commonly standard white light conditions do not allow for a strong discrimination between the different α -opic and the photopic lux.

Despite of this, tendencies to stronger relationships with melanopic lux were observed. In particular this was observed in the KSS output in which the largest correlation coefficients are found for the melanopic lux.

These tendencies were not observed in neither the cognitive performance tests or in the depression ratings. To what extent this is due to the quality of the available data cannot be fully portrayed. For instance, not in all literature on cognitive performance information was given about the light protocols (e.g. timing of lights on and lights off). On the other hand, light therapy for depression varies largely in the way it is applied (e.g., duration of exposure, duration of treatment, not a strict laboratory setting with not strict limitations on people's behavior).

In comparison to these two outputs, KSS and melatonin yielded more distinct results, also because the studies were methodologically better designed and provided more details about the light settings. Moreover, when considering melatonin suppression it becomes clearer that the quality of the data may indeed be of relevance. Melatonin suppression is a very well defined output and the most widely studied response in the NIF research. After the discovery that light can acutely suppress human melatonin levels (Lewy et al, 1980), suppression of melatonin by retinal light exposure has become a standard operating procedure for assessing NIF responses in humans. During light exposure, subjects usually sit quietly, keeping their eyes open with a fixed gaze. The data sets available for melatonin suppression were considerably larger than the ones existing for the other outputs. The data sets included a large amount of studies not only under wide conditions of light intensities but also under monochromatic light conditions. This allows for more proper photoreceptor weighted discrimination. As a matter of fact, the melatonin analysis shows that only when considering cyanopic, melanopic and rhodopic lux as light unit, a significant fit to the logistic model that describes melatonin suppression as a function of light dose is observed. Photopic lux showed no significant fit to the model.

Despite knowing that “melanopic lux” is not a unit, which is acceptable for lighting standards (i.e. it is not compliant to the SI system), and CIE already objected to its usage, we decided to use it here because of its wide acceptance in the scientific community. CIE recommended using only α -opic weighted irradiance, to be given in W/m², but we found that the comparability to the known photometric unit lx would be completely lost and practitioners who need to use such units in applications would be lost in energy-related units.

In the “HCL Toolkit” the new dimension “melanopic daylight equivalent illuminance” is introduced. The unit for this is lux and therefore it is SI-compliant as it refers to the photopic illuminance of daylight D65, which is the standardized spectral representation of natural daylight at 6500K. It allows comparing the ability of various light exposures to stimulate each of the five α -opic photoreceptors in relation to the ability of D65 to do the same. This parameter expresses the illuminance $E_{V,D65}$ of a light source with spectral characteristics of standard illuminant D65 that provides an α -opic irradiance $E_{e,\alpha,D65}$ that is identical to the α -opic irradiance $E_{e,\alpha,S}$ of light source S. As such, the quantity gives an impression of the amount of daylight that is needed to achieve the same α -opic irradiance as the current light condition of light source S.

When comparing different light sources for their ability to stimulate the melanopic channel it is useful to introduce in addition the concept of the melanopic daylight equivalent efficiency factor of luminous radiation (MDEF). MDEF denotes the ratio of the melanopic daylight equivalent illumination level (in lx) to the photopic illumination level (in lx) of a given light source. The melanopic daylight equivalent efficiency factor MDEF for different light sources is given in Table 3.

Some special considerations:

1. The α -opic daylight equivalent illuminance for standard illuminant D65 by definition equals the photopic illuminance expressed in lux for any of the potential five photoreceptors denoted by α .
2. For the case that α denotes melanopsin, the value of the melanopic daylight equivalent illuminance, for any arbitrary light source, is equal to the value of the "melanopic lux", according to Lucas et al., multiplied by the melanopic action factor for D65 of 0.906 which denotes the ratio of the melanopic weighted spectral power distribution to the photopic weighted spectral power distribution of a D65 light source. So the concepts of "melanopic lux" and melanopic daylight equivalent illuminance are comparable, except for the factor of 0.906, but the latter factor excludes conflicts with the existing SI system that needs to be respected in standards on light measurement.

Table 3: Melanopic daylight equivalent efficiency factor (MDEF) for different light sources.

illuminant	luminous flux [lx]	Melanopic illuminance (non SI compliant) [melanopic lux]	melanopic daylight equivalent illuminance [lx]	MDEF
D65 (daylight)	100	110.4	100	1
Fluorescent F11 (4000 K)	100	62.13	56.29	0.5629
LED warmwhite (3000 K)	100	45.0	40.76	0.4076
LED coolwhite (6500 K)	100	88.3	80.0	0.8
LED, blue (460 nm)	100	1073	972.1	9.721
LED, red (640 nm)	100	0.15	0.13	0.0013

CONCLUSION

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We conclude that, given the nature of this compilation, our observations do not come without limitations. The data included in the analysis of the different NIF responses differ in terms of quantity and quality. We observed that commonly used standard white light conditions do not allow for strong discrimination between α -opic and photopic irradiances.

However, as we add narrow bands and we introduce considerable changes in the spectral composition of light, we expect α -opic irradiances to be of great use in describing and predicting NIF responses. The use of α -opic irradiances to design light sources providing specific functions by including narrow spectral band sources and color temperatures to achieve, or avoid, certain NIF responses opens up opportunities for an accelerated uptake of solid-state lighting technology.

Despite the variability of the data considered in the meta-analysis the following preliminary conclusions can be drawn:

- The standard white light conditions as used in many scientific studies are inappropriate to decide which quantity from the five α -opic- and photopic irradiances is predictive for the light conditions ability to achieve NIF responses. For white light all these irradiances increase approximately linearly with the light intensity.
- So far the α -opic irradiances do not add much to discriminate between commonly used standard white light conditions. They are expected to be more useful predictors for NIF effects in more extreme light conditions (dim light, very low/high color temperature, or narrow band light,)
- Some NIF effects, like subjective alertness and the nocturnal suppression of the sleep-supporting hormone melatonin, seem to correlate more strongly with the melanopic irradiance (or melanopic lux) than with the photopic irradiance (expressed in lux). This is more enhanced when only considering those studies that use light with narrow spectral bands. The melatonin data (best quality and range of conditions) shows the impact of spectral distribution of light in which photopic lux fails to describe the response effectively.

Recommendations & Outlook

- It is recommended to start using α -opic irradiances and melanopic daylight equivalent illuminances as a metric to decide which light conditions can be used to promote, or avoid, certain NIF responses. The metric is expected to be particularly effective when designing light conditions with narrow spectral bands or different color temperatures.
- Healthy interior lighting requires dynamic indoor lighting designs that provide a high melanopic irradiance (or melanopic daylight equivalent illuminance) during daytime, especially in the morning. During the last 2 hrs before bedtime and at night, the light intensity (lux) and melanopic irradiance should be sufficiently dimmed to facilitate good sleep. With these inclusions, dynamic lighting strategies are a powerful tool to prevent sleep and body clock disturbances.

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6 | REFERENCES

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APPENDIX: LIGHT CHARACTERISTICS OF INCLUDED STUDIES

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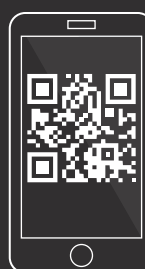
	Literature Source	N	Light Conditions	Light type	CCT (K)	Spectrum (± with peak)
KSS	Kräuchi 1997	9	5000 lx; Dim 8 lx	Fluorescent	4000 K	
	Cajochen 1998	8	5000 lx; Dim 8 lx	Fluorescent	4000 K	
	Rüger 2003	12	5000 lx Dim 10 lx	Fluorescent	5000 K	
	Cajochen 2005	10	12.1 µW/cm ² ; 10.1 µW/cm ² ; 0 lux	LED		460 (±10nm) 550 (±10nm)
	Rüger 2005	12 24	5000 lx Dim 10 lx	Fluorescent	5000 K	
	Lockley 2006	16	12.1 µW/cm ² ; 10.1 µW/cm ² ;	LED		460 (±10nm) 550 (±10nm)
	Cajochen 2011	13	110 lx 100 lx	Fluorescent LED	4775 K 6953 K	
	Smolders 2012	32	200 lx 4000 lx	Fluorescent	4600 K	
	Yokoi 2003	8	2800 lx 120 lx	Fluorescent	4000 K	
	Chellappa 2011	16	40 lx 40 lx 40 lx	Fluorescent	3000 K 6500 K 2500 K	
	Sivaji 2013	10	400 lux	Fluorescent	2700 K	
Melatonin suppression	Bojkowski et al. 1987	5	1,300, 2500 lux	Fluorescent	4000-5500 K	
	Brainard et al. 2001	72	0.03-100x10 ¹² photons/cm ²	Fluorescent		420-600 nm
	Brainard et al. 2015	24	1-800 µW/cm ²	Xenon arc lamp	4000 K, 17000 K	400-500 nm
	Cajochen et al. 2005	10	10.0-12.1 µW/cm ²	Fluorescent		460-550 nm
	Cajochen et al. 2011	13	100 lux	Xenon arc lamp		410-500 nm
	Hanifin et al. 2006	8	1.9x10 ¹⁸ photons/cm ²	LED, Fluorescent		460-700 nm
	Herljevic et al. 2005	34	3.8-62 µW/cm ²	Xenon arc lamp		456-560 nm
	Higuchi et al. 2007	10	1000 lux	Metal halide arc using Monochromatic filters	4200 K	
	Kozaki et al. 2008	12	200 lux	Fluorescent	2300-5000 K	
	Lavoie et al. 2003	14	bright white 300 lux; dim red <15 lux	Fluorescent	3500 K (assumed)	
	Lewy et al. 1980	6	500 lux; 1500-2500 lux	Fluorescent; Incandescent	3500 K (assumed); 2700 K (assumed)	
	Lockley et al. 2006	16	10.0-12.1 µW/cm ²	Xenon arc lamp		460-555 nm
	McIntyre et al. 1989	13	200-300 lux	Fluorescent	3500 K (assumed)	
	Phipps-Nelson et al. 2009	8	1 lux	LED		460-640 nm
	Revell & Skene 2007	11	2.1-10.4 µW/cm ²	Ultra high pressure Mercury lamp		479 nm
	Revell et al. 2010	12	19.1-36 µW/cm ²	Fluorescent	4000 K, 17000 K	437-532 nm
	Rüger et al. 2003	18	11.8 µW/cm ²	Xenon arc lamp		480 nm
	Santhi et al. 2011	22	225-700 lux	Fluorescent	4500 K (assumed)	
	Thapan et al. 2001	22	0.7-65.0 µW/cm ²	Metal halide arc using Monochromatic filters		424-548 nm
	Wahnschaffe et al. 2013	9	130 lux, 500 lux	Fluorescent, metal halogenid, dielectric inhibited	2000-6000 K	
	West et al. 2011	8	0.09-562 lux	blue LED; white fluorescent	4000 K	469 nm
	Whitmore et al. 2002	10	20-1000 lux	Fluorescent	3500 K (assumed)	530 nm
	Wirz-Justice et al. 2004	9	5000 lux	Fluorescent (assumed)	4000 K (assumed)	
	Wright & Lack 2001	15	130 µW/cm ²	LED		470-660 nm
	Wright et al. 2000	62	5000 lux	Halogen and light boxes	5000 K (assumed)	
	Wright et al. 2001	66	2000 lux	LED		460-560 nm
	Zeitzer et al. 2000	23	3-9100 lux	Fluorescent	3500 K (assumed)	

	Literature Source	N	Light Conditions	Light type	CCT (K)	Spectrum (± with peak)
d-2 Test	Barkmann 2012	116	1060 300	Fluorescent	5800 4000	
	Keis 2014	58	300	Fluorescent	5500 3500	
	Sleegers 2013 Study 1	98				
	Intervention Post		1000	Fluorescent	6500	
	Intervention Pre		300	Fluorescent	4000	
	Control Post		600	Fluorescent	4000	
	Control Pre		600	Fluorescent	4000	
	Study 2	44				
	Intervention Post		1000	Fluorescent	6500	
	Intervention Pre		350	Fluorescent	3000	
Depression rating	Control Post		380	Fluorescent	3000	
	Control Pre		380	Fluorescent	3000	
	Wessolowski 2010	90	1060 300	Fluorescent Fluorescent	6500 4000	
	Wessolowski 2009	116	1300 500	Fluorescent Fluorescent	5600 3200	
	Wirz-Justice et al. 2011 Control condition	16 11	7000 70	Fluorescent Fluorescent	5000	
	Martiny et al. 2009 Control condition	30 33	10000 50	Fluorescent Fluorescent	6000	
	Goel et al. 2005 Control condition	10 22	10000	Fluorescent Air ionisation	3000	
	Benedetti et al. 2003 Control condition	18 12	400	LED* Negative ion generator		500 / 485-515
	Corral et al. 2007 Control conditio	10 5	10000 600	Fluorescent Fluorescent	4000	
	Youngstedt et al. 2011 Control condition	17 16	3000	LED Negative ion generator	6000	460 and 550
	Paus et al. 2007 Control condition	18 18	7500 900	Fluorescent Fluorescent	6000	
	Braun et al. 1999 Control condition	16 18	10000 50	Fluorescent Fluorescent	5500	
	Martiny et al. 2005 Control condition	48 54	10000 50	Fluorescent Fluorescent	6000	
	Lee et al. 2013 Control condition	16 14	8000 5	LED LED		-/ 470-525 560 /-
	Royer et al. 2012 Control condition	15 13	400 75	LED LED		464 /- 628 /-
	Loving et al. 2005a Control condition	13 15	8500 10	Fluorescent Fluorescent	5000	
	Loving et al. 2005b Control condition	16 17	1200 50	LED LED		500 / 475-525 650 /-
	*Led not explicitly mentioned but assumed from given spectral					

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