Examining Eye-level Light Exposure Patterns and Human Sleep Behavior

Larissa Hunt

University of Colorado at Boulder

Department of Integrative Physiology

Defense Date: October 25, 2018

Thesis Committee:

Thesis advisor: Celine Vetter, Ph.D., Department of Integrative Physiology

Honors Council representative: Mark Opp, Ph.D., Department of Integrative Physiology

Third member: Lameese Akacem, Ph.D., Student Academic Success Center

Table of Contents

ABSTRACT

While laboratory studies have demonstrated that not only light exposure intensity, but also its duration, timing, and spectral composition are relevant for circadian physiology, most field studies examining links between light, circadian rhythms, sleep, and behavior rely on simple quantification of light intensity. Unpublished findings from the Circadian and Sleep Epidemiology Laboratory indicate that continuous light exposure levels of free-living individuals measured at the wrist are best captured by eight independent dimensions, represented by metrics including light intensity, timing, spectral composition, and the variability in timing of light exposure. However, wrist-level recordings of light have been shown to have error beyond relative measurement error, when compared to eye-level recordings. This study therefore uses eye-level light exposure data previously collected by Dr. Celine Vetter and colleagues in Munich, Germany to examine whether light exposure patterns measured at eye-level would show similar patterns as the light exposure patterns measured at wrist-level. K-means clustering algorithms were used to partition eye-level recordings (N=23, 5 days of recording) and results were compared to the wrist-level data from 2,154 individuals studied by Vetter et al (unpublished). Results indicate that light exposure profiles at eye-level are described by a similar set of patterns as those identified from wrist-level measurements, supporting the claim that light profiles are best represented by multiple independent dimensions. As a proof of principle, these different light dimensions identified were also found to have differential associations with chronotype as a model of individual sleep timing, and social jetlag as a model of circadian misalignment, both derived from MCTQ and sleep log data.

INTRODUCTION

The circadian system in humans regulates many parts of human physiology and behavior, and the timing of this system may shift due to input from environmental time cues. Intrinsically, human circadian rhythms can run independently from any environmental time cues[1], and intrinsic human circadian periods naturally vary on average between 24.2 hours and 24.9 hours[2]. However, in order to synchronize to the 24-hour light/dark cycle, the human circadian system actively entrains to the solar day by integrating information from rhythmic environmental stimuli, also called zeitgebers ("time-givers")[3]. Light is considered the most important zeitgeber for human circadian entrainment to the 24-hour day, and therefore, serves as the key synchronizing agent for the circadian system[4].

In order to quantify the effects of light on the human circadian system, researchers in laboratory studies examine how it can shift the timing of an individual's circadian phase, frequently marked by the onset of the hormone, melatonin[5,6]. This is regulated by the suprachiasmatic nucleus (SCN)[7] through norepinephrine release which acts upon the pineal gland causing it to release melatonin in the biological nighttime. If exposed to light at night, the SCN activates the retinohypothalamic tract suppressing norepinephrine and inhibiting melatonin, thereby shifting the timing of the circadian phase. Light affects the circadian system differently depending on the duration, intensity, spectral composition, timing, and history of light exposure an individual receives. The circadian system is most sensitive to long duration, high intensity light exposure as studies show the circadian phase shifts the most in response to longer durations and higher intensities of light[8,9]. Spectral composition also plays an important role in shifting the circadian phase, with shorter wavelengths of light resulting in the greatest phase delays[10], suggesting the human circadian system is the most sensitive to short wavelength light.

Additionally, the timing of light exposure can determine if the circadian phase will advance or be delayed. Light stimuli occurring at the beginning of an individual's biological nighttime result in maximum circadian phase delays, whereas light stimuli occurring at the end of the biological nighttime result in maximum circadian phase advances[11]. Studies also report that maximum phase delays occur in individuals exposed to a bright light after being in a dim light environment, suggesting the human circadian system is sensitive to prior light exposure[12]. Collectively, these reports demonstrate the importance of considering the many different dimensions of light when studying its effects on the human circadian system.

The timing of the circadian system in humans also helps to regulate sleep behavior. In terms of behaviors, this is especially evident with regards to sleep timing as the likelihood of being able to fall asleep is a function of time awake (or sleep pressure) as well as the circadian process, where sleep propensity follows a 24-hour rhythm. This interplay between sleep pressure and the circadian system has, for example, been modelled by the 2-process model of sleep regulation[13]. Predictions from this model suggest that sleep timing is at least in part dependent on circadian regulation. Processes that regulate sleep may be uncoupled either by forced desynchrony protocols in the laboratory or if the circadian system is not functional. This uncoupling greatly affects sleep homeostasis and can induce sleep fragmentation where the circadian system no longer helps sleep to follow a 24-hour cycle[14,15]. Normal functioning of the two processes that regulate sleep, on the other hand, results in a sleep/wake cycle that follows a roughly 24-hour period.

In humans, we observe large individual variability in sleep timing, which has in part been attributed to inter-individual differences in the underlying circadian period. In the field, researchers examine these inter-individual differences in sleep timing and categorize individuals

based on their sleep timing behavior, or chronotype, using the Munich ChronoType Questionnaire (MCTQ)[16]. The MCTQ determines chronotype by finding mid-sleep timing on free days (as these days are most representative of natural sleep behavior) and adjusts this time for sleep debt accumulated during the week. Because of the underlying circadian period, chronotype naturally varies between individuals; however, as shown in a study that examined sleep timing in individuals both at their homes in self-selected lighting, and after a week of camping in natural lighting[17], these variations can also become even more pronounced due to differences in lighting conditions. In the camping study, inter-individual differences in sleep timing were amplified when subjects were at home and allowed to self-select light exposure patterns, as the different light levels resulted in different timing shifts of the circadian system. Inter-individual differences in sleep timing decreased when individuals were camping and exposed to natural, uniform light exposure, as this entrained every individual to the same circadian timing, as compared to urban, self-selected light environments. Similar findings were found in a study that used mathematical modelling of human sleep and circadian physiology under natural conditions and realistic conditions that included electrical lighting[18]. The model found that variation in sleep timing doubled in the electrical condition (within the possible physiological range of entrainment). Additionally, this study found that if circadian periods were longer, the electrical condition resulted in a larger mismatch between workday/free day sleep timing, also referred to as social jetlag[19], which is associated with negative health outcomes such as obesity[20] and depression[21]. Taken together, these findings suggest that light exposure patterns influence the circadian system, and thereby individual sleep behavior. Therefore, the examination of these light exposure patterns is necessary, as they can have physiological and behavioral consequences in humans.

In field study settings, reports of light exposure patterns often focus on 24-hour averages of exposure brightness (lux). Because laboratory and field studies indicate the human circadian system and chronotype are sensitive to different dimensions of light, these reports of average brightness fail to capture the complexity of the relationship between different dimensions of light and the circadian system. Additionally, preliminary findings from the Circadian and Sleep Epidemiology Laboratory (CASE Lab) suggest light exposure profiles are best characterized by several, independent dimensions (Figure 1)[22]. Vetter et al. used machine learning algorithms, including k-means clustering, a partitioning method to decompose those light exposure profiles in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL, N = 2,154). The dimensions reported by Vetter et al. include duration and brightness of 24-hour light exposure, wavelength, nighttime light exposure, as well as timing of light exposure. Those light exposure patterns were measured using Philipps Actiwatch Spectrum devices, which record light and physical activity patterns at wrist-level. Because reports have shown that the accuracy and reliability of wrist-level light measures are limited, it remains unclear if these findings can be generalized to eye level measurements, as the eye is where light actively influences the circadian system[23].

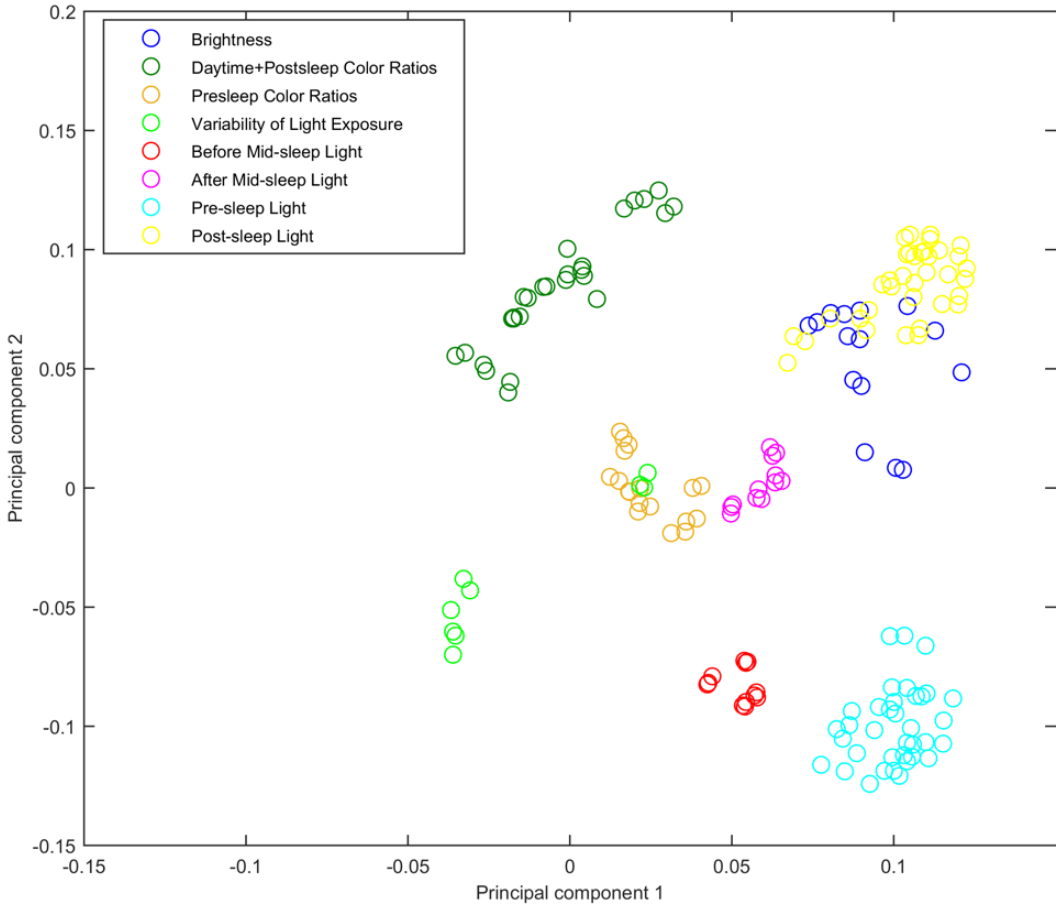

Figure 1: The eight independent dimensions of light that best characterize light exposure profiles measured at the wrist-level from preliminary findings by Vetter et al.[22] from the CASE Lab.

Aim 1 of this study is to address this gap in knowledge by decomposing eye-level light exposures and examining whether they are also best characterized by several dimensions. Although wrist-level light exposure recordings might have error, I hypothesize that overall characteristics of 24-hour light signals will show similar patterns over time, both at the eye and wrist-level. I therefore expect that eye-level light recordings would also be best reflected by several independent light dimensions, just as wrist-level recordings. In the case that this hypothesis has to be rejected, because eye-level data are best characterized by a completely dissimilar pattern of light exposure or by many fewer dimensions, understanding these discrepancies will inform the choice of light exposure assessments for any future studies. **Aim 2**

is to explore the association between identified light dimensions at eye-level and sleep behavior. Because the circadian system partly regulates sleep, I expect that sleep timing will be differentially affected by these light dimensions. I will consider average sleep duration, chronotype as a model of inter-individual differences in sleep timing[24], and social jetlag as a model of circadian misalignment[20]. Ultimately, this will help quantify eye-level light exposure as a modifiable environmental factor that can be leveraged for health and mood interventions associated with the human circadian system.

METHODOLOGY

Subject Population and Data Collection

Vetter and colleagues collected eye-level light exposure in 23 participants in autumn of 2015 in Munich, Germany. The Institutional Review Board of the Ludwig-Maximilian University of Munich approved the protocol. Participants aged 21-38 years old were included in the study (see Table 1 for further demographic characteristics). Subjects were pre-screened during an interview process and were excluded if they were shift workers, travelled across time zones, and/or suffered from any cataract disease, diabetes, or any pre-existing neurological disorder. Subjects completed two additional surveys, the first being the Munich ChronoType Questionnaire (MCTQ)[16] to determine their chronotype (MSFsc), as well as the Pittsburg Sleep Quality Index (PSQI)[25] to screen for any sleep abnormalities. Subjects maintained sleep logs throughout the study as a written record of their sleep timing, duration, and time spent outside.

Table 1: Participant characteristics.

Total N	23
Age (mean (sd))	29.35 (3.88)
Sex = Male (%)	9 (39.1)
BMI (mean (sd))	23.61 (5.01)
MSFsc (mean (sd))	4.22 (1.01)
Work Start Time (mean (sd))	8.64 (0.74)
Work End Time (mean (sd))	17.71 (1.21)
Work Duration (hrs) (mean (sd))	9.07 (0.90)

Data collection occurred in October of 2015, with five days of data collection prior, and five days following Daylight Savings Time (DST); I focus only on the data collection prior to DST (Friday-Tuesday). Light exposure was measured at eye-level by the Object-Tracker (OT)

LightWatcher data recorder, developed by Wolf Technologieberatung in Austria, attached to the frame of a pair of eyeglasses (Figure 2). This device measured eye-level light exposure in the red, green, and blue wavelengths every 10 seconds (epoch) for the entire period of data collection.

Figure 2: The OT LightWatcher data recorder attached to an eyeglasses frame. The OT LightWatcher data recorder measures eye-level light exposure in the red (620 nm), green (540 nm), and blue (465 nm) bands every 10 seconds.

Light Signal Processing

The partitioning methods used by the k-means clustering analysis require a wide range of variables as input. I therefore derived many variables from the light exposure profiles which would then later be used by the k-means clustering to identify which are the most relevant ones. I derived the identical variables as those used in Vetter et al that represent brightness, duration, wavelength, nighttime exposure, and timing of exposure of light (see Table 2 for full list). I derived average time spent above 100, 250, and 500 lux within the 24-hour day which is representative of the brightness of environmental light an individual is exposed to throughout the day. I quantified the wavelength characteristics of the light exposure profiles by the daytime ratio between the blue and green bands of the LightWatcher recordings. I derived both average brightness and blue to green wavelength ratios for 1-4 hours prior to habitual sleep onset and

following sleep offset. I also computed light exposure during the night for 10, 25, 50 and 100 lux. This was defined by the 4-hours prior and 4-hours past an individual's habitual mid-point of sleep. Finally, I determined timing of light exposure, best represented by a new metric proposed by Reid et al: MLiT, which is the mean timing of time spent above a given threshold (100/250/500 lux)[26].

In order to derive these variables, I adapted code generated using SAS® software[27] to open-source code generated using RStudio™ software[28]. The primary obstacle in the derivations was to manipulate the raw data file in order to create a few helper variables. I first created a midnight centered day for the daily average variables that were based on a rolling 24-hour day centered around midnight. I also created a noon centered day for the variables that required analysis of the full sleep period thus crossing midnight and necessitating a 24-hour day centered around noon. Additionally, because no white light measures were directly available, I estimated lux from the red, blue, and green wavelength channels collected by the sensor. Dr. Dieter Lang, a collaborator of the project who led the calibration procedure at OSRAM at the time of data collection, provided the equation to do so: lux ~ c*(0.381*R)+(0.954*G)+(0.074*B), where c is the calibration factor (constant, 0.683), R is the red light channel (620nm), G is the green light channel (540nm), and B is the blue light channel (465nm).

I used the midnight centered day to derive average daily brightness, daily color ratios, and MLiT. To derive daily brightness, I generated code to count the number of 10 second epochs above 100, 250, and 500 lux thresholds per day. I then back transformed this count into minutes to generate time above lux threshold per day. I used a similar technique to derive the daily color ratios of average blue to green ratios. However, instead of simply counting the number of 10 second epochs, I determined the blue to green ratio for each epoch and then averaged across the

day. I determined this average for multiple lux thresholds, namely 50, 100, 250, and 500 lux. The last midnight centered day variable derivation was MLiT, and was based on the technique used by Reid et al[26]. I first smoothed the raw data with a 10-minute moving average of lux and then I marked the epoch for each time this moving average exceeded a lux threshold of 100, 250, and 500 and determined the average time above each of these thresholds per day, thus producing the outcome of the mean daily time spent above threshold.

I used the noon centered day to derive all of the variables that consider sleep timing; these variables were average light at night, pre and post sleep color ratio, and the pre and post sleep light exposure. Light at night accounts for the amount of light an individual is exposed to in the time before their mid-sleep (mid-sleep time minus one half of the average habitual sleep duration ~ 4 hours), and the time after their mid-sleep (mid-sleep time plus one half of the average habitual sleep duration ~ 4 hours) and I calculated this for lux thresholds of 10, 25, 50 and 100 per night. I derived the color ratio and light exposure in the hours before and after sleep at the same time using very similar methods. I determined the average habitual sleep onset and offset for each subject, using data from the sleep logs, and then time periods for the one, two, three, and four hours before sleep onset and after sleep offset were determined. Then, I determined the average blue to green ratio along with the amount of time spent above lux thresholds of 10, 25, 50 and 100 for these periods before sleep onset and after sleep offset.

Table 2: Summary of derived light metrics.

Variable Set	Day	Description	Threshold (lux)
Daily brightness	Midnight centered	Average time spent above threshold	100, 250, 500
Daily color ratios	Midnight centered	Average blue:green ratio	50, 100, 250, 500
MLiT	Midnight centered	Mean timing of time spent above threshold	100, 250, 500
Light at night	Noon centered	Average time spent above threshold before and after mid-sleep	10, 25, 50, 100
Pre and post sleep color ratio	Noon centered	Average blue:green ratio in the 1, 2, 3 and 4 hours before sleep onset and after sleep offset	10, 25, 50, 100
Pre and post sleep light	Noon centered	Average time spent above threshold in the 1, 2, 3, and 4 hours before sleep onset and after sleep offset	10, 25, 50, 100

I calculated the mean, standard deviation, and mean absolute difference (MAD) for each variable I derived. I used the MAD measure to consider an additional quantification of light exposure variability daily, by determining the mean difference between consecutive days for each variable derived. This was calculated by finding the difference between values of every variable for each day and the day following it, moving through the time series.

After all the variables were generated, I took overall averages for each variable for each subject for valid days of collection. Valid midnight centered days included all days with less than four hours of missing data, and valid noon centered days included all days with less than 16% of the average sleep duration missing to ensure that the majority of sleep was measured so as to account for any light exposure during this time. Then, I analyzed each variable for percent missingness and zero values. As the missingness and zero levels were very low (<20%) for all of my data, and in order to be consistent with the variables used by Vetter et al., I chose to disregard

the missingness and zero percentages, so the final set of variables used in the identification of the light variables was the same as the set used by Dr. Vetter and colleagues in their original derivation.

K-means Clustering to Identify Light Dimensions

I performed a number of transformations on the variables in order for them to meet the assumptions of the k-means clustering analysis. I made Q-Q plots for every variable in order to visually examine the data for normality and skew of the distribution. Then, based on these Q-Q plots, I determined whether to either log transform, log(x+1) transform, or perform no transformation for each variable. I used log transformations for any variable with a non-normal distribution in the Q-Q plot and log(x+1) transformations for any variable with a non-normal distribution and a minimum of zero. These transformations ensured that each variable had a normal distribution. I then z-transformed each variable and by doing this, each variable was centered and scaled so that variables would carry equal weights for the k-means clustering analysis. I then transposed this final, transformed variable set as the intent of the k-means clustering was to cluster variables, and not subjects.

I performed the k-means clustering identification of light variables using code generated by MATLAB® software[29]. The code used a function for k-means clustering to analyze the transformed and transposed data. The function will try to fit the data to a certain number of clusters starting with one cluster and ending with a defined maximum number of clusters. It will try to fit each number of clusters, from one to the maximum number of clusters, for a pre-defined number of attempts (iterations); the higher the number of iterations, the more reliable the results. Here, I set the maximum number of clusters to 10, in line with Vetter et al.'s methodology, and I

set the number of iterations to 10,000. The key output that allowed me to judge the quality of the fitting procedures is the Aiken Information Criterion (AIC). This criterion quantifies the variability within a given cluster by determining the sum of squared differences from each data point to the centroid of each cluster. In line with prior work in the laboratory, the optimal number of clusters for this variable set was defined by the lowest AIC. In addition, k-means clustering quantifies how coherent a cluster is by computing a so-called silhouette value for each variable. Silhouette values are assigned on a scale from +1 to -1, with +1 indicating that a variable is very near to the center of its assigned cluster while simultaneously being far away from any other neighboring cluster, indicating how well the variable fits the cluster. Therefore, I selected the variable from each cluster with the highest silhouette value as the best representation of its given cluster.

In order to confirm and better visualize the results from the k-means clustering, I also generated a correlation matrix and performed a principal component analysis of the data using MATLAB® software. The correlation matrix is a visual representation of each individual point and the correlation between it and every other point in the set. These correlations are then graphed and color coded based on if they are positively correlated or negatively correlated with each other. The principal component analysis (PCA) is another method used to compress data. However, instead of creating clusters, it identifies principal components and then it visualizes the contribution of each variable to the components, resulting in different groupings.

Probing Associations with Sleep

I also examined the contribution of partitioning light profiles into several dimensions as no study to date has considered these dimensions concurrently. I analyzed the association between each

independent dimension of light identified by the k-means cluster, represented by one single variable, and average sleep duration, chronotype, and social jetlag using generalized linear models to estimate multivariable-adjusted mean differences in the respective outcomes and their 95% confidence intervals. I determined average sleep duration from the sleep logs subjects maintained during data collection by finding the difference between sleep onset and offset. Chronotype for each subject had already been previously determined by the MCTQ which measures mid-sleep time on free days and adjusts that time for accumulated sleep debt during the work week. Finally, I calculated social jetlag using data from the subject sleep logs by finding the difference between mid-sleep time on workdays and free days[20]. Before building the models I also visually examined each light metric using density and histogram distribution plots and after this examination of each metric, determined if each metric should be either categorical or continuous. The nighttime light metrics were best represented by categorical predictors, so I converted them to binomial variables with less than one lux of light exposure as the reference point.

I built three initial linear models using RStudio™ software for average sleep duration, chronotype, and social jetlag with each light metric as the exposure term. Initial models included sex as a covariate; the participant pool was relatively homogenous in all other aspects (see Table 1). I then developed parsimonious models to include only the exposure terms with p values less than 0.5 from the initial models. I also examined the distribution of the residuals from each model using Q-Q plots. The Q-Q plots showed a normal distribution of residuals and therefore no further transformations of the outcome variables were necessary. Finally, I computed the 95% confidence intervals for each light variable, and for both the initial and parsimonious models, respectively.

RESULTS

Light Dimensions

K-means clustering identified seven dimensions in eye-level light exposure profiles (Figure 3). The dimensions identified were brightness, pre-sleep color ratios, variability in light exposure, before mid-sleep light exposure, after mid-sleep light exposure, pre-sleep light exposure, and morning light exposure. Based on silhouette values of each variable attributed to a given cluster, I determined which single light variable would best represent a given cluster: the average daily light exposure above 250 lux for brightness dimension, the blue to green ratio exposure prior to sleep onset for the pre-sleep color ratios dimension, the variability in the blue to green ratio exposure prior to sleep onset for the variability dimension, the average daily time spent above 25 lux before mid-sleep for the before mid-sleep light exposure dimension, the average daily time spent above 100 lux after mid-sleep for the after mid-sleep light exposure dimension, the average daily time spent above 50 lux in the two hours prior to sleep onset for the pre-sleep light exposure dimension, and finally, the average daily time spent above 25 lux in the four hours following sleep offset for the morning light exposure dimension.

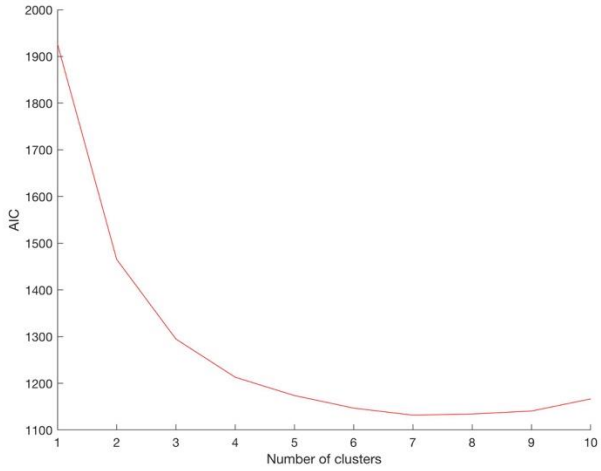

Figure 3: AIC type k-means clustering results. AIC values plotted from one to ten with a minimum AIC value at seven, and therefore, seven optimal clusters identified.

These results from eye-level continuous light recordings are similar but different because results found by Vetter et al. from wrist-level continuous light recordings identified eight independent dimensions of light (Table 3). However, the two levels of light recordings share seven of the same identified independent dimensions of light (brightness, pre-sleep color ratios, variability in light exposure, before mid-sleep light exposure, after mid-sleep light exposure, pre-sleep light exposure, and morning light exposure) with the wrist-level results containing one extra dimension (daytime and morning color ratios).

Table 3: Summary of identified light dimensions and the most representative variable of each dimension at eye-level, compared to wrist-level

Cluster	Top Variable	Silhouette Value
Brightness		
Eye-Level	Daily light exposure above 250 lux	0.36
Wrist-Level	Daily light exposure above 500 lux	0.55
Pre-sleep Color Ratios		
Eye-Level	Pre-sleep blue:green ratio	0.4
Wrist-Level	Pre-sleep blue:green ratio	0.57
Variability in Light Exposure		
Eye-Level	Variability in pre-sleep blue:green ratio	0.51
Wrist-Level	Mean light timing (MLiT) above 250 lux	0.75
Before Mid-sleep Light Exposure		
Eye-Level	Before mid-sleep light exposure above 25 lux	0.78
Wrist-Level	Before mid-sleep light exposure above 25 lux	0.79
After Mid-sleep Light Exposure		
Eye-Level	After mid-sleep light exposure above 100 lux	0.48
Wrist-Level	After mid-sleep light exposure above 50 lux	0.6
Pre-sleep Light Exposure		
Eye-Level	Light exposure above 50 lux 2 hours before sleep onset	0.95
Wrist-Level	Light exposure above 25 lux 3 hours before sleep onset	0.66
Morning Light Exposure		
Eye-Level	Light exposure above 100 lux 4 hours after sleep offset	0.77
Wrist-Level	Light exposure above 25 lux 3 hours after sleep offset	0.51
Daytime & Morning Color Ratios		
Wrist-Level	Post-sleep blue:green ratio	0.54

The silhouette values (SIL) for each variable of each identified dimension of light from eye-level recordings indicate three very coherent clusters: before mid-sleep light with an average SIL of 0.68 and top variable SIL of 0.78, pre-sleep light exposure with an average SIL of 0.92 and top variable SIL of 0.95, and finally, morning light exposure with an average SIL of 0.63 and top variable SIL of 0.76. These clusters are also consistent when looking at the most representative variables of the eye-level vs. wrist-level light recordings results, as the main differences exist in the lux thresholds (pre-sleep light exposure - 50 lux vs. 100 lux; post-sleep light exposure – 100 lux vs 25 lux) and the number of hours (pre-sleep light exposure – 2 hours vs. 3 hours; post-sleep light exposure – 4 hours vs. 3 hours). For the remaining four clusters the silhouette values indicate more variability within clusters and a less optimal fit for the most representative variables: brightness with an average SIL of 0.15 and top variable SIL of 0.36, pre-sleep color ratios with an average SIL of 0.20 and top variable SIL of 0.40, variability in light exposure with an average SIL of 0.25 and top variable SIL of 0.51, and after mid-sleep light with an average SIL of 0.36 and top variable SIL of 0.52. However, these results are consistent with the wrist-level recordings results for most representative variables, with the exception of the variability in light exposure cluster. Where the best fit for eye-level exposure was variability in pre-sleep blue to green ratio and the best fit for wrist-level exposure was mean light timing above 250 lux. Taken together, these results support the hypothesis that eye-level light exposure can be described by a similar pattern as the pattern found by Vetter et al. at wrist level.

The results from the correlation matrix are also similar to the results found by the k-means clustering analysis (Figure 4). There are a few areas of the correlation matrix with very strongly positive correlated variables (bright yellow sections), namely the before mid-sleep, after mid-sleep, pre-sleep, and parts of the morning variables. This is consistent with the higher

silhouette values for the corresponding light dimensions for these variables found during the k-means clustering. The correlation matrix also shows areas of negative correlations (dark blue) spread throughout some of the less tightly correlated groupings of variables: brightness, color ratios, MLiT, and pre-sleep and morning color ratios. Again, these correlations are consistent with the k-means clustering silhouette values of the corresponding dimensions of light as these groupings tended to include variables that were sorted by the k-means into the weaker clusters of light dimensions.

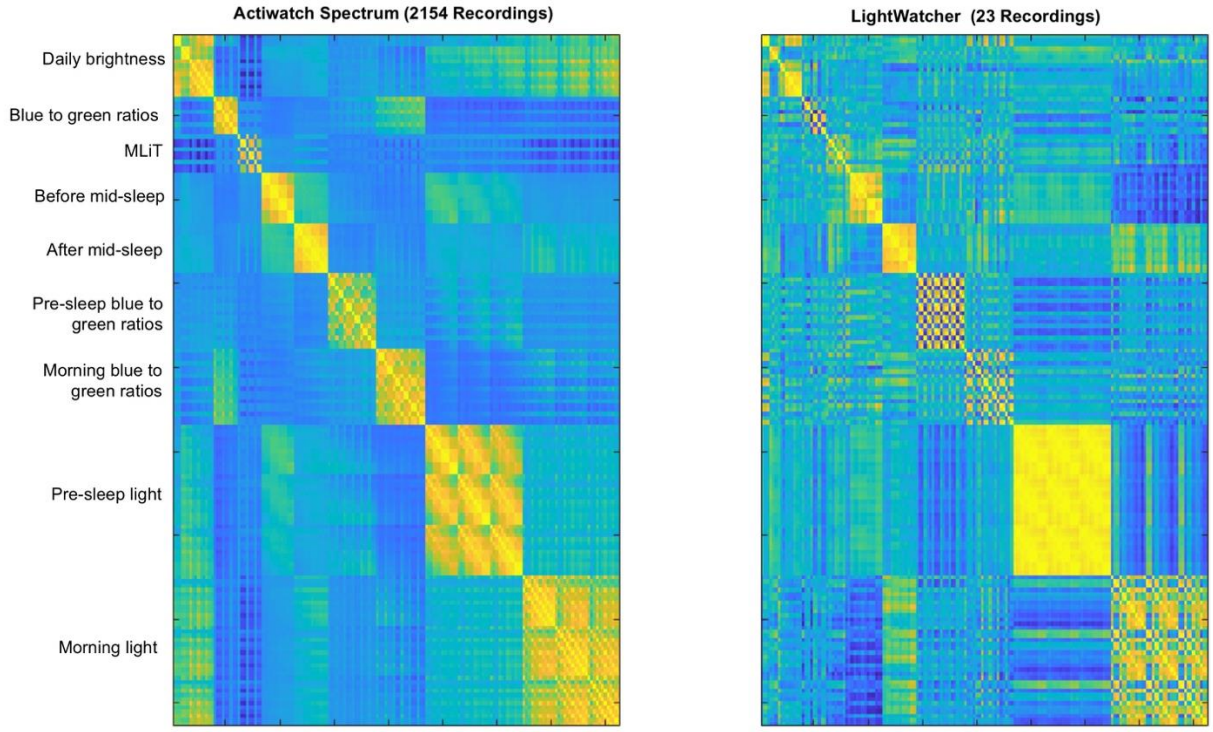

Figure 4: Correlation matrices of light metrics derived from wrist-level (left) and eye-level (right) continuous recordings of light exposure. Yellow indicates a positive correlation and blue indicates a negative correlation.

Additionally, when comparing the correlations to the same variables generated by wrist-level light measurements (Figure 4), the correlation matrices of both eye-level and wrist-level light show similar patterns to those from the k-means clustering. It is evident that the correlation

between the eye-level light variables are in general similar to those same variables from wrist-level light. However, there is also much more noise, and clearer negative correlations within clusters when examining the eye-level light variable correlation matrix as compared to the wrist-level correlation matrix. This is consistent with the generally lower silhouette values of the eye-level light dimensions compared to wrist-level light dimensions identified by the k-means, which indicates greater variability within clusters and more possible correlations between clusters. The final observation worth noting from the correlation matrix is the difference between the correlations of the pre-sleep light variables of both eye-level and wrist-level light. In contrast to the general increased noise in the rest of the eye-level correlation matrix, the pre-sleep light exposure variables are all very highly, positively correlated and even more so than the same variables in the wrist-level matrix. Collectively, all of the observations from the correlation matrices support and visually validate the k-means clustering analysis findings.

The findings of the PCA (Figure 5) also support the results generated by the k-means clustering analysis and shows the grouping and variability within and between clusters. It is clear from the PCA that there are four distinct groupings (before mid-sleep light, after mid-sleep light, pre-sleep light, and morning light) with little variability within them and high distinction from other clusters. Although the silhouette value determined by the k-means clustering for the after mid-sleep light exposure cluster was only 0.48, the PCA suggests this cluster is actually quite robust and distinctive from the others; however, as the PCA is only a two-dimensional model of the principal components, further analysis of the three-dimensional principal components would be necessary to validate this. The remaining three clusters (brightness, pre-sleep color ratios, and variability in light exposure) are highly variable within groups and less distinguishable from

others, consistent with both the k-means clustering analysis and the patterns seen in the correlation matrix.

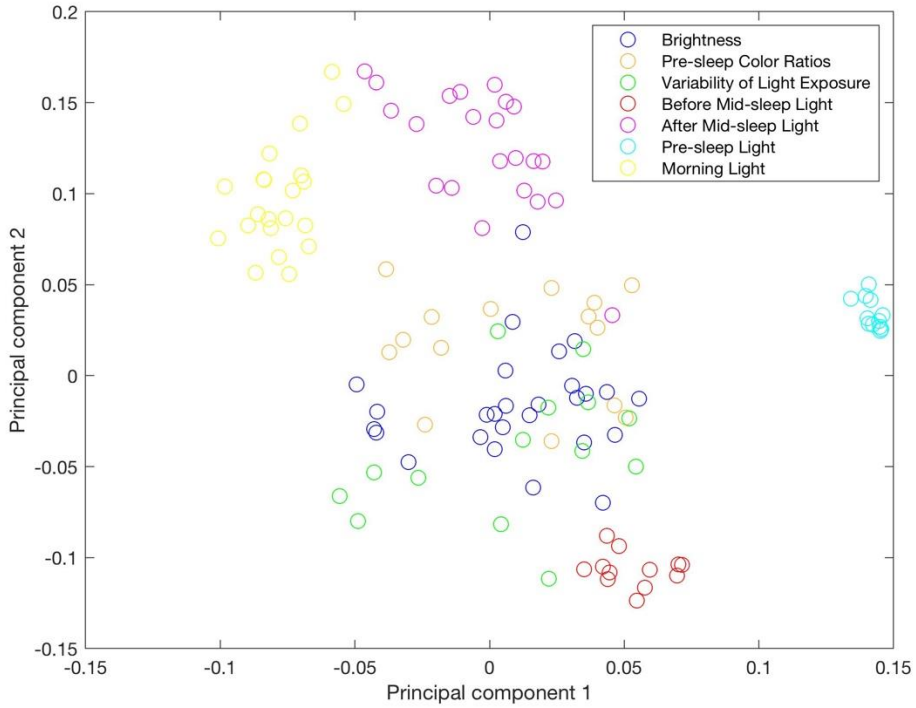

Figure 5: Graphical representation of the results of the principal component analysis of eye-level continuous light recordings.

Light Dimensions and Sleep

Secondary analysis served to demonstrate the usability and necessity of deriving and identifying different light dimensions by building linear models to probe for associations between the light metrics and average sleep duration, chronotype as a model of inter-individual differences in sleep timing, and social jetlag as a model of circadian misalignment for the 23 participants of the study. Surprisingly, of all the possible associations between the different light dimensions and the three sleep outcomes only two significant associations were found (see Tables 5, 6, and 7 for full results). Before mid-sleep light exposure was found to be associated with chronotype, and after mid-sleep light exposure was found to be associated with social jetlag. Specifically, any

time spent above 25 lux in the ~4 hours before mid-sleep was associated with a later chronotype (by 1.12 hours, 95% CI: 0.36;1.87, p<0.01), and any time spent above 100 lux in the ~4 hours after mid-sleep was associated with greater social jetlag (by 0.68 hours, 95% CI: 0.08;1.28, p<0.05). It is also worth noting a few other dimensions of light that, despite not being significant, seemed to have very large effect estimates with some of the sleep outcomes. For example, higher pre-sleep blue to green color ratio was associated with longer average sleep duration (by 1.37 hours, 95% CI: -2.16; 4.91), and later chronotype (by 0.80 hours, 95% CI: -4.41;6.00). Additionally, based on the results from the parsimonious model of social jetlag, sex had a large effect on social jetlag (by -0.50 hours, 95% CI: -1.11;0.11). Overall, regardless of the general lack of significant associations found by the regression models, these results still support the claim that it is necessary to derive and identify these different dimensions of light as even just the two associations found show the different effects different dimensions of light can have on sleep related outcomes.

Table 5: Summary of multivariable linear models for average sleep duration.

Model	Estimate	95% Confidence Intervals	
		Lower	Upper
Initial			
Daily light exposure above 250 lux	0.19	-0.12	0.51
Pre-sleep blue:green ratio	1.37	-2.16	4.91
Variability in pre-sleep blue:green ratio	0.25	-0.73	1.23
Before mid-sleep light exposure above 25 lux	-0.07	-0.66	0.53
After mid-sleep light exposure above 100 lux	-0.47	-1.16	0.22
Light exposure above 50 lux 2 hours before sleep onset	0.52	-0.36	1.41
Light exposure above 100 lux 4 hours after sleep offset	0.00	-0.03	0.03
Sex	0.16	-0.56	0.87
Parsimonious			
Daily light exposure above 250 lux	0.22	-0.05	0.48
Pre-sleep blue:green ratio	1.10	-1.73	3.94
After mid-sleep light exposure above 100 lux	-0.44	-0.95	0.07
Light exposure above 50 lux 2 hours before sleep onset	0.38	-0.12	0.88

Estimates are in hours of sleep duration. *p < 0.05, **p < 0.01

Table 6: Summary of multivariable linear models for chronotype.

Model	Estimate	95% Confidence Intervals	
		Lower	Upper
Initial			
Daily light exposure above 250 lux	-0.33	-0.79	0.14
Pre-sleep blue:green ratio	0.80	-4.41	6.00
Variability in pre-sleep blue:green ratio	0.14	-1.30	1.58
Before mid-sleep light exposure above 25 lux	1.18*	0.31	2.06
After mid-sleep light exposure above 100 lux	-0.30	-1.32	0.72
Light exposure above 50 lux 2 hours before sleep onset	-0.46	-1.76	0.84
Light exposure above 100 lux 4 hours after sleep offset	0.03	-0.01	0.07
Sex	0.32	-0.74	1.38
Parsimonious			
Daily light exposure above 250 lux	-0.28	-0.67	0.11
Before mid-sleep light exposure above 25 lux	1.12**	0.36	1.87
Light exposure above 50 lux 2 hours before sleep onset	-0.49	-1.24	0.26
Light exposure above 100 lux 4 hours after sleep offset	0.03	-0.01	0.07

Estimates are in hours of chronotype. *p < 0.05, **p < 0.01

Table 7: Summary of multivariable linear models for social jetlag.

Model	Estimate	95% Confidence Intervals	
		Lower	Upper
Initial			
Daily light exposure above 250 lux	-0.07	-0.42	0.27
Dre-sleep blue:green ratio	-0.57	-4.43	3.30
Variability in pre-sleep blue:green ratio	0.06	-1.01	1.13
Before mid-sleep light exposure above 25 lux	0.30	-0.35	0.95
After mid-sleep light exposure above 100 lux	0.61	-0.15	1.36
Light exposure above 50 lux 2 hours before sleep onset	-0.01	-0.98	0.95
Light exposure above 100 lux 4 hours after sleep offset	0.01	-0.03	0.04
Sex	-0.42	-1.20	0.37
Parsimonious			
Before mid-sleep light exposure above 25 lux	0.26	-0.27	0.79
After mid-sleep light exposure above 100 lux	0.68*	0.08	1.28
Sex	-0.50	-1.11	0.11

Estimates are in hours of social jetlag. *p < 0.05, **p < 0.01

DISCUSSION

The aim of this study was to identify the independent dimensions of light that best characterized eye-level light exposure profiles, and to see how well the eye-level patterns compare to wrist-level patterns characterized by Vetter et al. To do so, I decomposed eye-level light exposure profiles for 23 individuals to generate a wide range of variables that represented the brightness, duration, wavelength, nighttime exposure, and timing of light exposure for each individual. I then used k-means clustering analyses to partition these variables to determine which are most representative of each light dimension. The k-means clustering analysis identified seven independent dimensions: brightness, pre-sleep color ratios, variability, before mid-sleep, after-mid-sleep, pre-sleep, and morning light exposure, suggesting I should not reject my hypothesis that eye-level light exposure patterns are characterized similarly to wrist-level light exposure patterns. As a proof of principle, I also probed the associations between the identified light dimensions and average sleep duration, chronotype, and social jetlag. Light exposure before mid-sleep was associated with later chronotype, and light exposure after mid sleep was associated with greater social jetlag.

Eye-level vs. Wrist-level Dimensions of Light

Light exposure measured at eye-level was found to best represented by seven independent dimensions of light: brightness, pre-sleep color ratios, variability of, before mid-sleep, after mid-sleep, pre-sleep, and morning light exposure. Vetter et al., also found these same seven, plus an eighth, independent dimensions of light to be representative of light exposure measured at wrist-level. The eighth independent dimension of light identified from wrist-level measurements is the daytime and morning color ratio of light. Although this dimension was not identified in this

study from eye-level measurements of light exposure, the results from the k-means clustering analysis, correlation matrix, and PCA indicate the possibility that this eighth dimension could still be identified by eye-level measurements. The k-means clustering analysis from this study of light metrics derived from eye-level light exposure found seven optimal dimensions of light, however, as shown in Figure 3, this optimal could easily be represented by eight dimensions of light as well. This is supported by the amount of variability and the weak correlations within the color ratios and morning color ratios groupings of the correlation matrix for eye-level light exposure. This pattern can also be seen in the PCA showing the low cohesiveness of the pre-sleep color ratio and variability of light exposure which both contain some of the light variables that belong to this wrist-level dimension (see Appendix Table 8 for full list of variables in each cluster). Taken together, these results indicate the possible existence of an eighth dimension of eye-level measurements of light.

The other inconsistency between the eye-level and wrist-level derived light metrics is in the variability dimension of light exposure. This study, using eye-level measurements of light, identified this variability dimension with the most representative variable being the variability in pre-sleep blue to green ratios. This same dimension was identified by analysis of wrist-level measurements of light, but, was best represented by the light metric MLiT. In fact, the eye-level variability dimension was not a strong cluster, indicated by patterns seen in both the correlation matrix and the PCA, and additionally, the k-means clustering analysis indicated that the variability in pre-sleep blue to green ratio light metric is not a strong fit to this specific dimension (SIL = 0.51). This all suggests that despite any inconsistency in this variability dimension of light identified, variability in light exposure is an important dimension of light to

be considered, and it remains to be determined exactly what metric this dimension is best represented by at the eye-level.

Many of the other minor inconsistencies between the eye-level and wrist-level derived dimensions of light could potentially be explained by returning to the differences between the locations of measurement. Measurements of light exposure made at the wrist-level can potentially carry error, specifically when it comes to measurements of light during the nighttime. At night, the wrist area of the body is frequently covered by bed sheets or clothing leading to a higher amount of missing data and a less accurate representation of the true light exposure an individual receives at night. This could contribute to the lower representation of sleep derived light metrics from wrist-level light measurements as compared to eye-level wrist measurements. Similarly, this could explain the robustness of the nighttime light exposure dimensions of light made by measurements at the eye-level and the higher variability in these same dimensions from wrist-level measurements of light exposure. Light also hits the wrist area of the body at a different angle than it would hit an individual's eye, this difference in angle has been found to overestimate bright light exposure during the daytime and underestimate shorter wavelength, dimmer light[23]. This could account for some of the differences in lux for the most representative light metrics of each dimension and also contribute to differences in representation of night time light exposure when short wavelength becomes more important. Regardless of any differences between the dimensions of light derived from eye-level measurements vs. wrist-level measurements, this study found that light is best represented by multiple, independent dimensions, and ultimately, this is consistent with similar patterns found by Vetter et al. using wrist-level measurements of light.

As this study aimed to compare the different dimensions of light identified by eye-level measurements of light and by wrist-level measurements of light, the largest limitation of this part of the study was the lack of direct comparison between subjects for these two levels of measurement. Eye-level measurements of light used in this study were obtained from a very small, homogenous subject pool (n = 23). Wrist-level measurements of light used to identify light dimensions were made by Vetter et al. from a much larger subject pool (n = 2,154) as part of the HCHS/SOL study. Given this, the subject pool differences are quite evident and therefore a direct comparison between the two is impossible. In order to address this limitation, it would be useful to run a future study that collects light data at both the eye-level and wrist-level to be able to make direct comparisons. In fact, the CASE Lab is in the process of obtaining IRB approval to conduct a study that will do just that by collecting close to eye-level and wrist-level light data and hopefully provide the data needed to be able to make these direct comparisons.

A few other limitations of the primary aim of the study include the small sample size (n = 23), the known differences of patterns of missingness and of zeros between eye-level and wrist-level light measurements, and the overemphasis of variability. As mentioned above, this study used a very small, homogenous subject pool for measurements of light at the eye-level. This small sample size may be another limitation of this study as this decreases the reliability of any findings and decreases statistical power. In terms of the limitation due to different patterns of missingness and zero values, this effect was seen primarily when choosing the final list of derived light metrics to be used in the k-means clustering analysis. To be consistent with the list of metrics used by Vetter et al. for the k-means analysis of wrist-level measurements, this study used the same list despite knowledge of differences in patterns of missingness. This could have skewed the results as, because of these differences, the eye-level light dimensions might have

been differently represented if different metrics were included/excluded. Both of these limitations could be addressed in the study soon to be conducted by the CASE Lab as we should have more subjects and days of recording and be able to better compare the missingness and zero values between the two locations of measurement. Finally, by including both standard deviations and MADs of all light metrics, both this study and the study conducted by Vetter et al. possibly overemphasized light variability. This limitation remains to be addressed by re-analysis of the data by exclusion of the extra variability measures or inclusion of median measures for all metrics.

Light Dimensions and Sleep

The identified light dimensions were found to only have a few significant associations with the sleep outcomes. Before mid-sleep light exposure was associated with later chronotype and after mid-sleep light exposure was associated with greater social jetlag. These findings are both consistent, and can be explained by the circadian response curves to timing of light exposure: light exposure at the beginning of an individual's biological nighttime induces circadian timing delays and thus shifts chronotype (i.e., sleep timing) later, and light exposure at the end of an individual's biological nighttime induces circadian timing advances which could decrease sleep duration thus increasing sleep debt and ultimately, social jetlag[11]. In fact, the association can also be explained by the reverse relationship as findings are consistent with self-selected light exposure patterns of later chronotypes. Individuals with later sleep timing are more likely to select more light exposure later in the evening and receive higher levels of light exposure when they awake[24] . Later chronotypes (i.e., individuals with later sleep timing) are also more likely to have greater amounts of social jetlag[19] as their preferred timing does not align well with social

obligations and work schedules, forcing them to awake closer to their average mid-sleep time and thereby exposing them to more light during this time. Collectively, these findings and the results from the regression models are consistent with previous studies and indicate the necessity of considering the different dimensions of light as they can help explain different patterns in light exposure of individuals with differing sleep behavior.

Although not significant, a few other larger effects were seen from the results of the regression models when examining the associations. The effect estimates for blue to green ratios and suggest a relationship between higher blue to green ratios with longer sleep duration and later chronotype. The longer sleep duration could likely have been a result of reduced sleep quality as this would necessitate more sleep time to achieve the same results. This is consistent with the findings by a study that found that evening use of blue light emitting electronic devices left individuals feeling sleepier and less rested in the morning[30]. If given the chance, these individuals might have slept longer in order to feel more rested. Additionally, this blue light exposure in the evening can induce circadian timing delays thus explaining the association with later chronotype. The effect estimate for female sex also suggests a possible relationship with lower social jetlag. This is not surprising because females are more likely to be earlier chronotypes in their adult years[31], and earlier types tend to be less susceptible to sleep debt as social constraints and work obligations align better with their preferred sleep wake schedules[20].

Despite being consistent with findings from other studies, the effects of these variables and all other variables that had no significant associations cannot be truly known until more studies are conducted. The small sample size of this study (n = 23) contributed to the lack of associations as it greatly decreases the power of this study and thus makes it difficult for associations to be significant. Using data soon to be collected in the pilot study by the CASE

Lab, it will be possible to re-analyze the relationship between the different dimensions of light and sleep behavior with an increased number of participants.

Overall, despite the small sample limitation, the examination of the association between the dimensions of light and human sleep behavior served to gain a more accurate understanding of the effect of the different dimensions of light on sleep behavior. The complexity of this relationship is important to understand as abnormal sleep behavior, and in particular chronic sleep debt, can lead to circadian misalignment. Circadian misalignment is associated with obesity[20,32], type two diabetes[33], and coronary heart disease[34]. These negative health outcomes are due in part to disruptions in an individual's circadian rhythm which is an important regulator of body temperature[35], blood pressure[36], and insulin sensitivity[37]. By better understanding light exposure patterns and their associations with the circadian system and sleep, we can learn about potential avenues to improve and target interventions for physiological and behavioral disorders that are connected to the circadian system and thereby, might be responsive to light as a therapeutic method.

CONCLUSION

The partitioning methods used in this study identified seven independent dimensions that best represent continuous recordings of eye-level light exposure, as compared to the eight dimensions identified by Vetter et al. that represent light exposure measured at the wrist-level. The seven dimensions of light exposure identified from eye-level recordings of light are consistent with seven, of the eight, dimension of light exposure identified from wrist-level recordings of light. Results from both measurements suggest the importance of average daily brightness, color ratios, variability, before mid-sleep, after mid-sleep, pre-sleep, and morning measurements of light exposure. The similarities between the eye-level and wrist-level light exposure patterns suggest that light exposure, regardless of where it is measured, is best represented by multiple, different dimensions. These findings support the results of previous studies that found different dimensions of light need to be considered, and also indicate a need for more research on light exposure in order to fully represent the different dimensions of light exposure that can be used for studies of relationship between light exposure patterns and the circadian system, health, and sleep behavior in humans.

REFERENCES

1. Czeisler C, Gooley J. *Sleep and Circadian Rhythms in Humans*. Vol 72.; 2007. doi:10.1101/sqb.2007.72.064

2. Czeisler CA, Duffy JF, Shanahan TL, et al. Stability, Precision, and Near-24-Hour Period of the Human Circadian Pacemaker. *Science*. 1999;284(5423):2177-2181. doi:10.1126/science.284.5423.2177

3. Pandi-Perumal SR, Trakht I, Srinivasan V, et al. Physiological effects of melatonin: Role of melatonin receptors and signal transduction pathways. *Prog Neurobiol*. 2008;85(3):335-353. doi:10.1016/j.pneurobio.2008.04.001

4. Czeisler CA, Richardson GS, Zimmerman JC, Moore-Ede MC, Weitzman ED. Entrainment of Human Orcadian Rhythms by Light-Dark Cycles: A Reassessment. *Photochem Photobiol*. 1981;34(2):239-247. doi:10.1111/j.1751-1097.1981.tb08993.x

5. Benloucif S, Burgess HJ, Klerman EB, et al. Measuring Melatonin in Humans. *J Clin Sleep Med JCSM Off Publ Am Acad Sleep Med*. 2008;4(1):66-69.

6. Pandi-Perumal SR, Smits M, Spence W, et al. Dim light melatonin onset (DLMO): A tool for the analysis of circadian phase in human sleep and chronobiological disorders. *Prog Neuropsychopharmacol Biol Psychiatry*. 2007;31(1):1-11. doi:10.1016/j.pnpbp.2006.06.020

7. RALPH MR, FOSTER RG, DAVIS FC, MENAKER M. Transplanted Suprachiasmatic Nucleus Determines Circadian Period. 2018;247:5.

8. Chang A-M, Santhi N, St Hilaire M, et al. Human responses to bright light of different durations. *J Physiol*. 2012;590(Pt 13):3103-3112. doi:10.1113/jphysiol.2011.226555

9. Zeitzer JM, Dijk D-J, Kronauer RE, Brown EN, Czeisler CA. Sensitivity of the human circadian pacemaker to nocturnal light: melatonin phase resetting and suppression. *J Physiol*. 2000;526(Pt 3):695-702. doi:10.1111/j.1469-7793.2000.00695.x

10. Wright HR, Lack LC. Effect of light wavelength on suppression and phase delay of the melatonin rhythm. *Chronobiol Int*. 2001;18(5):801-808.

11. Khalsa SBS, Jewett ME, Cajochen C, Czeisler CA. A phase response curve to single bright light pulses in human subjects. *J Physiol*. 2003;549(Pt 3):945-952. doi:10.1113/jphysiol.2003.040477

12. Chang A-M, Scheer FAJL, Czeisler CA. The human circadian system adapts to prior photic history. *J Physiol*. 2011;589(Pt 5):1095-1102. doi:10.1113/jphysiol.2010.201194

13. Daan S, Beersma DG, Borbely AA. Timing of human sleep: recovery process gated by a circadian pacemaker. *Am J Physiol-Regul Integr Comp Physiol*. 1984;246(2):R161-R183. doi:10.1152/ajpregu.1984.246.2.R161

14. Naylor E, Bergmann BM, Krauski K, et al. The Circadian Clock Mutation Alters Sleep Homeostasis in the Mouse. *J Neurosci*. 2000;20(21):8138-8143. doi:10.1523/JNEUROSCI.20-21-08138.2000

15. Franken P, Dijk D-J. Circadian clock genes and sleep homeostasis. *Eur J Neurosci*. 2009;29(9):1820-1829. doi:10.1111/j.1460-9568.2009.06723.x

16. Roenneberg T, Wirz-Justice A, Merrow M. Life between Clocks: Daily Temporal Patterns of Human Chronotypes. *J Biol Rhythms*. 2003;18(1):80-90. doi:10.1177/0748730402239679

17. Stothard ER, McHill AW, Depner CM, et al. Circadian Entrainment to the Natural Light-Dark Cycle across Seasons and the Weekend. *Curr Biol*. 2017;27(4):508-513. doi:10.1016/j.cub.2016.12.041

18. Swaminathan K, Klerman EB, Phillips AJK. Are individual differences in sleep and circadian timing amplified by use of artificial light sources? *J Biol Rhythms*. 2017;32(2):165-176. doi:10.1177/0748730417699310

19. Wittmann M, Dinich J, Merrow M, Roenneberg T. Social Jetlag: Misalignment of Biological and Social Time. *Chronobiol Int*. 2006;23(1-2):497-509. doi:10.1080/07420520500545979

20. Roenneberg T, Allebrandt KV, Merrow M, Vetter C. Social jetlag and obesity. *Curr Biol CB*. 2012;22(10):939-943. doi:10.1016/j.cub.2012.03.038

21. Levandovski R, Dantas G, Fernandes LC, et al. Depression Scores Associate With Chronotype and Social Jetlag in a Rural Population. *Chronobiol Int*. 2011;28(9):771-778. doi:10.3109/07420528.2011.602445

22. Vetter C, Phillips AJK, Reid KJ, et al. Decomposing Light Exposure Profiles and their differential associations with Obesity and Depressive Symptoms.

23. Figueiro MG, Hamner R, Bierman A, Rea MS. Comparisons of three practical field devices used to measure personal light exposures and activity levels. *Light Res Technol Lond Engl 2001*. 2013;45(4):421-434. doi:10.1177/1477153512450453

24. Roenneberg T, Merrow M. Entrainment of the Human Circadian Clock. *Cold Spring Harb Symp Quant Biol*. 2007;72:293-299. doi:10.1101/sqb.2007.72.043

25. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research. *Psychiatry Res*. 1989;28(2):193-213. doi:10.1016/0165-1781(89)90047-4

26. Reid KJ, Santostasi G, Baron KG, Wilson J, Kang J, Zee PC. Timing and Intensity of Light Correlate with Body Weight in Adults. Mistlberger RE, ed. *PLoS ONE*. 2014;9(4):e92251. doi:10.1371/journal.pone.0092251

27. *SAS Software © 2016 SAS Institute Inc., Cary, NC, USA. Reprinted with Permission. All Rights Reserved.*

28. *RStudio Team (2016). RStudio: Integrated Development for R. RStudio, Inc., Boston, MA URL Http://Www.Rstudio.Com/.*

29. *MATLAB and Statistics Toolbox Release 2018a, The MathWorks, Inc., Natick, Massachusetts, United States.*

30. Chang A-M, Aeschbach D, Duffy JF, Czeisler CA. Evening use of light-emitting eReaders negatively affects sleep, circadian timing, and next-morning alertness. *Proc Natl Acad Sci U S A*. 2015;112(4):1232-1237. doi:10.1073/pnas.1418490112

31. Roenneberg T, Kuehnle T, Juda M, et al. Epidemiology of the human circadian clock. *Sleep Med Rev*. 2007;11(6):429-438. doi:10.1016/j.smrv.2007.07.005

32. Fonken LK, Workman JL, Walton JC, et al. Light at night increases body mass by shifting the time of food intake. *Proc Natl Acad Sci U S A*. 2010;107(43):18664-18669. doi:10.1073/pnas.1008734107

33. Vetter C, Dashti HS, Lane JM, et al. Night Shift Work, Genetic Risk, and Type 2 Diabetes in the UK Biobank. *Diabetes Care*. 2018;41(4):762-769. doi:10.2337/dc17-1933

34. Vetter C, Devore EE, Wegrzyn LR, et al. Association between rotating night shift work and risk of coronary heart disease among women. *JAMA*. 2016;315(16):1726-1734. doi:10.1001/jama.2016.4454

35. Saarela S, Reiter RJ. Function of melatonin in thermoregulatory processes. *Life Sci*. 1994;54(5):295-311.

36. Simko F, Paulis L. Melatonin as a potential antihypertensive treatment. *J Pineal Res*. 2007;42(4):319-322. doi:10.1111/j.1600-079X.2007.00436.x

37. la Fleur SE, Kalsbeek A, Wortel J, van der Vliet J, Buijs RM. Role for the pineal and melatonin in glucose homeostasis: pinealectomy increases night-time glucose concentrations. *J Neuroendocrinol*. 2001;13(12):1025-1032.

APPENDIX

Table 8: Supplemental material of all light metrics derived at eye-level and included in k-means clustering analysis, correlation matrix, and PCA including cluster assignments, silhouette values, and the overall light dimension.

Light Metric	Cluster	Silhouette Value	Dimension
avg_dailytalt_250	1	0.360807981	Average brightness
mad_dailytalt_250	1	0.349527523	
sd_dailytalt_500	1	0.346686834	
sd_whitelight	1	0.325589687	
avg_dailytalt_500	1	0.316842147	
sd_postsleep4bluegreenratio_10	1	0.312315094	
avg_whitelight	1	0.307753673	
sd_dailytalt_250	1	0.306564558	
mad_dailytalt_500	1	0.28391942	
mad_whitelight	1	0.272902097	
sd_postsleep3bluegreenratio_10	1	0.211423359	
sd_postsleep4bluegreenratio_25	1	0.177782705	
sd_bluegreenratio_250	1	0.129131807	
mad_dailytalt_100	1	0.123317446	
mad_bluegreenratio_100	1	0.115181663	
mad_bluegreenratio_250	1	0.108504761	
sd_postsleep3bluegreenratio_25	1	0.10601007	
sd_bluegreenratio_500	1	0.09412584	
sd_postsleep2bluegreenratio_10	1	0.092194437	
sd_bluegreenratio_100	1	0.04488757	
mad_postsleep4bluegreenratio_25	1	0.044866179	
mad_bluegreenratio_500	1	0.031288063	
mad_postsleep3bluegreenratio_25	1	0.025019952	
mad_postsleep3bluegreenratio_10	1	0.017077485	
sd_dailytalt_100	1	0.004071644	
mad_postsleep4bluegreenratio_10	1	-0.071286976	
avg_dailytalt_100	1	-0.208480155	
avg_presleep3bluegreenratio_25	2	0.400135014	Pre-sleep color ratios
avg_presleep2bluegreenratio_25	2	0.400132126	
avg_presleep4bluegreenratio_25	2	0.400130157	
avg_presleep2bluegreenratio_10	2	0.377607726	
avg_presleep4bluegreenratio_10	2	0.377605527	
avg_presleep3bluegreenratio_10	2	0.377604798	
avg_postsleep2bluegreenratio_10	2	0.271780506	
avg_postsleep4bluegreenratio_25	2	0.231440216	
avg_postsleep3bluegreenratio_25	2	0.22905072	
avg_postsleep4bluegreenratio_10	2	0.2119779	
avg_mlit_500	2	0.18947901	
mad_medianwhitelight	2	0.181666389	
avg_postsleep2bluegreenratio_25	2	0.154056732	

avg_mlit_250	2	0.117397718	
avg_postsleep3bluegreenratio_10	2	0.060437592	
avg_mlit_100	2	0.033270806	
sd_medianwhitelight	2	-0.003714587	
avg_bluegreenratio_100	2	-0.026077329	
avg_medianwhitelight	2	-0.179675338	
sd_presleep3bluegreenratio_10	3	0.514112514	Variability in light exposure
sd_presleep4bluegreenratio_10	3	0.514110809	
sd_presleep2bluegreenratio_10	3	0.514109237	
sd_presleep4bluegreenratio_25	3	0.502083636	
sd_presleep2bluegreenratio_25	3	0.502083307	
sd_presleep3bluegreenratio_25	3	0.502078506	
mad_presleep2bluegreenratio_10	3	0.375736546	
mad_presleep3bluegreenratio_10	3	0.375733198	
mad_presleep4bluegreenratio_10	3	0.375727	
sd_mlit_500	3	0.218768	
mad_presleep4bluegreenratio_25	3	0.16531625	
mad_presleep3bluegreenratio_25	3	0.165315008	
mad_presleep2bluegreenratio_25	3	0.165311895	
mad_mlit_500	3	0.151519802	
mad_mlit_250	3	0.122387107	
sd_mlit_250	3	0.098938701	
avg_bluegreenratio_500	3	0.094257557	
sd_mlit_100	3	0.087335418	
mad_postsleep2bluegreenratio_25	3	0.085010362	
mad_postsleep2bluegreenratio_10	3	0.080222398	
mad_mlit_100	3	0.021769458	
avg_bluegreenratio_250	3	-0.06147038	
avg_beforemidsleep_talt_25	4	0.781181981	Before mid-sleep light exposure
sd_beforemidsleep_talt_50	4	0.763454868	
mad_beforemidsleep_talt_50	4	0.757083314	
avg_beforemidsleep_talt_50	4	0.753260845	
avg_beforemidsleep_talt_10	4	0.721634146	
mad_beforemidsleep_talt_25	4	0.718280481	
mad_beforemidsleep_talt_10	4	0.670368153	
sd_beforemidsleep_talt_10	4	0.640651819	
sd_beforemidsleep_talt_100	4	0.629572969	
mad_beforemidsleep_talt_100	4	0.618775696	
sd_beforemidsleep_talt_25	4	0.567452233	
avg_beforemidsleep_talt_100	4	0.547147273	
mad_postsleep4_n_25	5	0.522153912	After mid-sleep light exposure
sd_postsleep4_n_25	5	0.51996966	
mad_aftermidsleep_talt_50	5	0.502886312	
sd_aftermidsleep_talt_100	5	0.499734338	
mad_aftermidsleep_talt_100	5	0.49162807	
mad_postsleep3_n_25	5	0.487048904	
avg_aftermidsleep_talt_100	5	0.479855124	

mad_aftermidsleep_talt_25	5	0.478056712	
sd_aftermidsleep_talt_50	5	0.472132792	
sd_postsleep3_n_25	5	0.449876307	
sd_aftermidsleep_talt_25	5	0.442908939	
avg_aftermidsleep_talt_25	5	0.437406317	
avg_aftermidsleep_talt_50	5	0.414633295	
mad_postsleep4_n_10	5	0.397562625	
sd_aftermidsleep_talt_10	5	0.387601681	
sd_postsleep2_n_10	5	0.387199149	
mad_postsleep2_n_10	5	0.38359763	
mad_postsleep2_n_25	5	0.377891661	
mad_postsleep3_n_10	5	0.353983565	
mad_aftermidsleep_talt_10	5	0.326472296	
sd_postsleep3_n_10	5	0.324797458	
avg_aftermidsleep_talt_10	5	0.306859197	
sd_postsleep2_n_25	5	0.269400918	
sd_postsleep4_n_10	5	0.237753821	
mad_postsleep4_n_50	5	0.1518193	
sd_postsleep2bluegreenratio_25	5	0.10046319	
mad_postsleep3_n_50	5	0.031560666	
sd_postsleep4_n_50	5	-0.060562878	
avg_presleep2_n_50	6	0.947700875	
avg_presleep3_n_50	6	0.94769787	
avg_presleep4_n_50	6	0.947693474	
avg_presleep4_n_25	6	0.943967122	
avg_presleep3_n_25	6	0.943964324	
avg_presleep2_n_25	6	0.943962052	
mad_presleep4_n_50	6	0.926254465	
mad_presleep2_n_50	6	0.92625335	
mad_presleep3_n_50	6	0.926252142	
avg_presleep3_n_100	6	0.925638466	
avg_presleep4_n_100	6	0.925636974	
avg_presleep2_n_100	6	0.925634057	
sd_presleep4_n_50	6	0.92010959	
sd_presleep2_n_50	6	0.92010876	
sd_presleep3_n_50	6	0.920101632	
sd_presleep4_n_25	6	0.919615701	
sd_presleep2_n_25	6	0.919615452	
sd_presleep3_n_25	6	0.919612868	
avg_presleep2_n_10	6	0.917926413	
avg_presleep3_n_10	6	0.917919051	
avg_presleep4_n_10	6	0.917918789	
mad_presleep4_n_100	6	0.91505662	
mad_presleep3_n_100	6	0.915052513	
mad_presleep2_n_100	6	0.915051378	
sd_presleep2_n_100	6	0.904296437	
sd_presleep3_n_100	6	0.904291485	

Pre-sleep light exposure

sd_presleep4_n_100	6	0.904290526	
sd_presleep4_n_10	6	0.903747402	
sd_presleep3_n_10	6	0.903746922	
sd_presleep2_n_10	6	0.903737936	
mad_presleep3_n_25	6	0.902304549	
mad_presleep2_n_25	6	0.902304104	
mad_presleep4_n_25	6	0.902301665	
mad_presleep3_n_10	6	0.876997187	
mad_presleep4_n_10	6	0.876994129	
mad_presleep2_n_10	6	0.876991429	
avg_postsleep4_n_25	7	0.768048939	
avg_postsleep3_n_100	7	0.761986889	
avg_postsleep3_n_25	7	0.757321205	
avg_postsleep4_n_50	7	0.73872459	
avg_postsleep4_n_100	7	0.73684348	
avg_postsleep4_n_10	7	0.726098573	
avg_postsleep3_n_50	7	0.72386632	
avg_postsleep2_n_25	7	0.720710879	
mad_postsleep2_n_100	7	0.720247365	
avg_postsleep2_n_50	7	0.711910118	
avg_postsleep3_n_10	7	0.706083464	Morning light exposure
avg_postsleep2_n_100	7	0.697729931	
sd_postsleep3_n_100	7	0.668365767	
sd_postsleep2_n_100	7	0.647791659	
mad_postsleep3_n_100	7	0.636487995	
avg_postsleep2_n_10	7	0.62853464	
sd_postsleep4_n_100	7	0.580824432	
mad_postsleep4_n_100	7	0.484609717	
sd_postsleep2_n_50	7	0.352409021	
mad_postsleep2_n_50	7	0.27830499	
sd_postsleep3_n_50	7	0.217694819	