Metabolic implications of polychromatic LED and OLED light exposures at night

(夜間の LED と OLED 照射がエネルギー代謝に及ぼす影響)

2021

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School of Integrative and Global Majors in University of Tsukuba

Ph.D. Program in Human Biology

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博　士（人間生物学）学　位　論　文

Ph.D. Dissertation in Human Biology

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Acknowledgements

I would first like to thank my supervisors, Professor Kumpei Tokuyama, who has guided me and advised me every step of the way during my doctoral studies, and Professor Masashi Yanagisawa, for his insightful comments and continuous support. I would also like to express my sincere gratitude to my dissertation committee, Professor Hitoshi Shimano, Dr. Kaspar Vogt, Professor Yu Hayashi, and Dr. Takashi Abe. Their astute feedback and critical questions helped to elevate the quality of my work.

I greatly appreciate the support I received from the collaborative work with Professor Junji Kido and Professor Takeshi Sano at the Yamagata University. I am particularly grateful for their invaluable feedback during our discussions and for providing me with their immense expertise and knowledge in conducting experiments using organic LED. I also wish to thank the technical support I received from Mr. Yuki Abe of the Organic Lighting Corporation.

I would also like to extend my sincere gratitude to Dr. Makoto Satoh and Dr. Momoko Kayaba for their guidance and support at the earlier stage of my doctoral studies, sharing their knowledge and expertise in conducting sleep studies. I am also very grateful for the support and meaningful feedback I obtained from Dr. Insung Park, Dr. Yoko Suzuki, Dr. Katsuhiko Yajima, Ms. Simeng Zhang, and other members in the lab who have contributed by helping to collect and analyze my data. And of course, a big thank you to all the research participants who have cooperated in the experiment.

Finally, my heartfelt thank you to my family members, Kozue, Toshikazu, Miyabi, and Satori Ishihara, for their unconditional support, especially during this very intense academic year. I am grateful to all who have kept me positive and engaged in completing this journey.

Abstract

Light pollution, or excessive light at nighttime, has become a global concern across various species. Exposure to light at night has been reported in numerous studies to induce alterations in sleep and circadian rhythm. Similarly, epidemiological studies have indicated an increase in the risk of weight gain and obesity from excessive light at night. However, little has been studied on the effects of light at night on energy metabolism during sleep. Additionally, the spread of the use in light-emitting diode (LED), rich in short wavelengths of blue light (455nm), has been suspected to be linked with the negative impacts on human physiology. In the present study, LED exposure at night was compared with the organic light-emitting diode (OLED) using organic compounds in the light-emitting layer, allowing illumination from a surface source with less glare and blue content in the emission from polychromatic light. Ten healthy males (25.7 ± 0.65 years; 22.3 ± 0.65kg/m^2) participated in the study with exposures to four continuous hours of LED, OLED, or dim light (<10 lux) before sleep in a metabolic chamber room. Sleep architecture assessed from EEG activity did not differ significantly among the light conditions. Energy expenditure and core body temperature significantly declined during sleep under OLED compared with dim light conditions ($p<0.001$). Following exposure to LED, respiratory quotient was significantly higher ($p=0.016$), and fat oxidation was significantly reduced ($p=0.001$) compared with OLED during sleep. Although there was no correlation between LED and the concentration of urinary 6-sulfatoxymelatonin, exposure to OLED showed a positive correlation between the two, suggesting that the role of melatonin in lipolysis may differ depending on the light. These results provide a further understanding of the role of light on energy metabolism during sleep and suggest the potential usage of OLED to mitigate the negative consequences of exposure to light at night.

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Abbreviations

ALAN	Artificial light at night
aMT6s	6-sulfatoxymelatonin
DPG	Distal-proximal gradient
DLMO	Dim light melatonin onset
EEG	Electroencephalogram
ipRGC	Intrinsically photosensitive retinal ganglion cells
KSS	Karolinska sleepiness scale
LED	Light-emitting diode
NREM	Non-rapid eye movement
OLED	Organic light-emitting diode
PSG	Polysomnography
REM	Rapid eye movement
RHT	Retinohypothalamic tract
RQ	Respiratory quotient
SCN	Suprachiasmatic nucleus
SWS	Slow-wave sleep
VLPO	Ventrolateral preoptic area

Chapter 1: Introduction

1.1 Artificial light at night

Artificial light at night (ALAN) has effectively extended human activity around the world during dark hours. However, with great development, comes great consequences. In 2016, approximately 83% of the world's population was living under light-polluted skies, ranging from nonpolluted areas such as 0.12% of Greenland and 0.29% of Central African Republic to 58% of Argentina, 66% of South Korea, 98% of Kuwait, and most light-polluted country being Singapore (Falchi et al., 2016). Inhabitants of countries living under extreme light pollution cannot fully dark-adapt their eyes to night vision (Falchi et al., 2016). Thus, health consequences due to excessive light exposure at dark hours have been of significant concern.

Light pollution in the form of ALAN has spread worldwide, impacting animal behavior and plant physiology, influencing various aspects of the environment and ecology. For instance, domestic pigeons (Columba livia) and Australian magpies (Cracticus tibicen tyrannica) sleep less, favor non-rapid eye movement sleep compared to rapid eye movement sleep, and have more fragmented sleep under light exposure in the evening compared to no light at night (Aulsebrook et al., 2020). Many other studies have reported increased night-time activity (Ulgezen et al., 2019; Aulsebrook et al., 2020) and earlier onset of daily activity in diurnal animals (de Jong et al., 2017; Kempenaers et al., 2010) due to the rise in exposure to ALAN. Additionally, the behavioral pattern of bats, such as foraging, commuting, emergence, roosting, breeding, hibernation, and abundance, has been studied to be impacted by ALAN (Khan et al., 2020; Voigt et al., 2016). Nestling and hatchlings of sea turtles occur at night, but in some instances, spawning at sea and abandonment of nests occurred with coastal light (Falcón et al., 2020). Plant-aphid-parasitoid communities were also affected by slight changes in light intensity at night (Sanders et al., 2018), suggesting a broader implication of ALAN on living organisms.

1.2 Evolution of light

The evolution of light began at the early stages of civilization when human beings used fire for torches, then oil lamps, and candles. However, a fire had its constraints for safety issues and excessive heat production when increasing light levels. The invention of artificial light addressed these limitations and allowed illumination of the streets during dark hours. In the 19th century, the development of incandescent lamps started to take place, one of which Thomas Edison invented the first practical incandescent light bulb in 1879 (Marshall et al., 2016). Since then, artificial light has continued to transform from incandescent to fluorescent bulbs to light-emitting diodes (LEDs) (Marshall et al., 2016) (Fig. 1).

In Japan, efforts to decarbonize and achieve a carbon-neutral society by 2050 have been addressed in the principles of green innovation by the Ministry of Economy, Trade, and Industry (METI). One of the proposed approaches to tackle environmental issues is in infrastructure. Through this approach, they aim to address the importance of increasing the use of energy-efficient LED and organic light-emitting diodes (OLED), simultaneously reducing the production and usage of fluorescent and mercury lamps (Japan's Green Innovation, n.d; LED 2019). For this reason, it is crucial to understand the physiological impacts and potential risks of LED and OLED.

1.3 Light-emitting diodes and organic light-emitting diodes

Since the invention of LEDs in the 1960s, they have developed to replace previously implemented less efficient light sources. From uses in calculators and digital watches, the usage of LED has spread to displays, automotive and aerospace lighting, traffic signals, and optical communications, demonstrating diverse applications of LEDs in our daily lives (Nardelli et al., 2017).

An LED is composed of a p-n junction and a semiconductor diode which are layered, ultimately emitting energy in the form of light from the contact between the electrical potential of anode and cathode (Fig. 2). The chemical composition of semiconductors determines the wavelength and color of light, where semiconductors with an energy gap lying between 1.7 and 3 eV emit light in the visible region (Chitnis et al., 2016). The advantage of using an LED is that it consumes less power by operating on low driving voltages and currents, allowing a lifespan to be around 35,000 to 50,000h

of usage, and thus, reducing its operating expenses (Chitnis et al., 2016). The high-speed response time enables on-off within a microsecond, without requiring excessive heat to produce light. They also do not produce UV or infrared components, making them cost and energy-efficient sources of light. The conventional LEDs, however, had various obstacles to be confronted. Such were the problems of glare from the point-light source because of small lamp size, dependence on ambient temperature, relatively high color temperature, and its cause for blue light pollution that directly affects the physiology of living organisms (Almeida et al., 2014; Chitnis et al., 2016). It is noteworthy that advances in LEDs today address these limitations, enabling the production of lights that emit warm white to cool color temperatures and LEDs with reduced blue light (LightingEurope, 2016; SORAA, 2017). One such example of blue reduced light is the BlueFree SSL technology developed by Soraa, producing white LEDs by replacing the blue with violet light. This light stimulus at an illuminance of 35 lux induced greater pupil dilation immediately after the light was turned off, compared to standard LEDs containing a blue spectrum of light (David, 2017, unpublished). Another example tackling this issue is through dynamically changing light (dynLED) with an incrementally increasing color temperature and illuminance in the morning and decreases gradually from noon to evening. Compared to static LED (sLED) with consistent color temperature throughout the day at 4000K, dynLED did not attenuate melatonin levels in the evening and induced significantly shorter sleep latency (Stefani et al., 2020). Although more studies are needed to understand the optimal light condition for physiological health, progress made in the LED industry aims to improve and elevate the currently implemented light systems.

In recent years, OLED has gained popularity mainly in the application of flat panel displays such as TVs and electronic devices. The basic structure of OLED and LED are similar except for the organic, carbon-based materials utilized in OLED as a layer between the anode and cathode (Fig. 2). Substrate material that serves as a deposition of light from all layers in OLED is often made of glass or plastic to allow transparency and flexibility of the light. OLEDs generally have a wide viewing angle, allowing for a surface light source compared to the LEDs with a point-light source. (Chitnis et al., 2016). The quality of white light is evaluated based on several parameters, one of them being the correlated color temperature (CCT). CCT is correlated with the wavelength such that low CCT

(<2800K) consists of longer wavelengths of red light, whereas shorter wavelengths such as blue light are linked with higher CCT (>6500K) (Sliney et al., 2016). OLED can reach a color temperature as low as 1773K, equivalent to that of candles (Jou et al., 2014), aiming to work against the potential damages to the retinal cells from a spectrum rich in blue light (Jou et al., 2017). Although it was proposed that OLED lights tend to have a shorter life span compared to LEDs, displays using OLED light have also been demonstrated to extend their lifespan to 100,000 hours (Larsen, 2016). Rapid growth in the use of advanced technology in the light industry calls for an up-to-date, careful investigation of physiological health.

1.4 Role of light on human physiology

Light has a profound influence on human physiology including sleep-wake regulations (Cajochen et al., 1992), circadian rhythm (Czeisler et al., 1986), mood and cognition (Czeisler et al., 1990; Bedrosian et al., 2017), thermoregulation (Cajochen et al., 2005), and endocrine systems (Lewy et al., 1980; Jun et al., 2010). Light is initially detected by the photoreceptors in the retina including rods, cones, and intrinsically photosensitive retinal ganglion cells (ipRGCs). Where rods and cones are primarily responsible for image-forming responses to light, ipRGCs are responsible for the non-image-forming functions such as circadian regulations. ipRGCs express the photopigment melanopsin, which is most sensitive to short wavelengths of blue light (~480nm) while showing minimal effect at the longer wavelength of red light (>600nm) (Brainard et al., 2001). Photic information integrated by the ipRGCs is transmitted to the central circadian oscillators, the suprachiasmatic nucleus (SCN), via the retinohypothalamic tract (RHT) (Gooley et al., 2001). ipRGCs are also known to project to other areas of the hypothalamus and the subcortical limbic zone, which include lateral geniculate complex, habenular regions, superior colliculus, olivary pretectal nucleus, preiaqueductal gray, and the ventrolateral preoptic area (VLPO) (Hattar et al., 2006) (Fig. 3).

The role of ipRGCs on circadian regulation was confirmed when photic stimulation entrained circadian responses and maintained melatonin suppression even in the absence of rods and cones (Berson et al., 2002; Lucas et al., 1999). However, in melanopsin deficient mice, rods and cones function to entrain light cycles in order to compensate for the loss of melanopsin, but at lesser degree

(Ruby et al., 2002). The function of ipRGCs, along with rods and cones is crucial in understanding the influence of light on different parts of the brain.

1.5 LED and OLED light exposure on sleep and circadian rhythm

Investigation into the physiological effects of LED have focused on its spectral power distribution that differs greatly from previously established fluorescent light sources. In humans, 2000 lux of blue/green LED resulted in significant melatonin suppression and greater delay in dim light melatonin onset (DLMO) but not in white LED, suggesting that the phase shift in melatonin was more effective in blue/green LED (Wright et al., 2008). Exposure to the narrow bandwidth of blue LED in the evening was especially effective in suppressing melatonin and promoting subjective and objective alertness at night (West et al., 2011; Figueiro et al., 2004; Figueiro et al., 2007). Additionally, evening use of light-emitting eReaders (peak irradiance at 450nm) before sleeping reduced melatonin secretion, inducing circadian phase delay, along with an increase in objective alertness before sleep and prolonged sleep latency (Chang et al., 2014). A different study also reported sustained alertness from the reduction in slow eye movement and EEG low-frequency activity after 5 hours of computers with light-emitting diode displays in the evening (Cajochen et al., 2011). Together, the consensus of LED emitting peak spectral content at approximately 450nm is known to delay the circadian rhythm by suppressing melatonin and promoting alertness.

OLED, on the other hand, is known to emit less blue light and has been suspected to be more physiologically friendly compared to LED. Park and colleagues exposed participants to 150 lux (4000K) LED and OLED light 6.5 hours prior to sleep and reported that melatonin onset was more delayed under LED compared with OLED (Park et al., 2020). In a follow-up to this study, light exposure to 150 lux (3000K) of LED and OLED resulted in a significant delay in melatonin onset under LED compared with OLED and a lower percentage in slow-wave sleep (Jo et al., 2021). Although these studies suggest that OLED may impact sleep and the circadian rhythm less severely compared with LED due to the reduction in blue light, it is still premature to conclude any general ideas about its physiological effects, such as body temperature and energy metabolism on humans.

1.6 Thermoregulation

Besides sleep and circadian regulations, light has been documented to influence core body and skin temperature. Body temperature is well connected to the circadian rhythm such that light administered before the circadian nadir that occurs during sleep induces phase delay, whereas light exposure after the nadir time advances the phase of circadian rhythm (Czeisler et al., 1995). It is also linked to sleep and alertness behavior where exposure to bright light (2500 lux) 3 hours prior to sleep resulted in a significant increase in core body temperature from 1 hour before sleep and 4 hours into sleep, along with the increase in sleep onset compared with the dim light condition (6 lux) (Dijk et al., 1990). It was also reported that light exposure (> 500 lux) between 21:00 and 23:00 after melatonin onset significantly increased body temperature before the onset of sleep, suggesting its alerting effect on sleep (Myers et al., 1993). Additionally, exposure to monochromatic blue light (460nm) and green light (550nm) in comparison to the control with no light 2 hours in the evening before sleep resulted in a significant increase in body temperature during and after light exposure, suggesting the wavelength dependency on the alerting effect of light measured from body temperature (Cajochen et al., 2005; Münch et al., 2006).

Although core body temperature decline is associated with the initiation of sleep, so is the rise in skin temperature from proximal and distal regions throughout the body. Elevation in skin temperature is accompanied by vasodilation of distal skin regions. Kräuchi and colleagues summarized various interventions such as light exposure and exogenous melatonin administration could alter responses in skin temperature, and most importantly act on the regulation of sleep by inducing vasodilation (Kräuchi et al., 1999). Additionally, ingestion of ice subsequently resulted in a decline in the core body temperature. However, instead of inducing sleepiness, alertness was augmented, along with a reduction in distal skin temperature followed by vasoconstriction (Kräuchi et al., 1999). For this reason, it is essential to understand the functions of thermoregulation in relation to other physiological parameters aside from sleep which are influenced by exposure to light.

1.7 Energy metabolism

The impact of light exposure at night extends beyond human sleep and circadian rhythm. Many epidemiological studies have indicated the association between light exposure and increased body weight and risk of obesity (Danilenko et al., 2013; Obayashi et al., 2013; McFadden et al., 2014). In one study, following the completion of 7-day food log of caloric intake, sleep log, and light monitoring using a wrist actigraphy, exposure to light (> 500 lux) at later meantime was associated with higher BMI (Reid et al., 2014). Shift work exposes individuals to high intensity of light at night which has been linked to higher BMI and increased risk of type 2 diabetes (van Drongelen et al., 2011; Pan et al., 2011). Consistent with this result, bright light (>500 lux) at night was associated with an increase in plasma glucose and insulin, suggesting glucose intolerance and insulin insensitivity due to extended light at night (Albreiki et al., 2017).

However, less is known about the impact of light on energy metabolism, especially on energy expenditure and substrate oxidation. In individuals with seasonal depression, morning light exposure treatment has been shown to either lower (Gaist et al., 1990) or cause no significant immediate effect on resting metabolic rate (Ivanova et al., 2016). Similarly, among individuals with seasonal depression, daytime light treatment (2500 lux) between 14:00 and 16:00 for one week effectively increased the consumption of oxygen (Pinchasov et al., 2000). In healthy participants, 750 lux of daytime light exposure for a continuous 14 hours from 8:00 showed no significant impact on 24h energy expenditure or substrate oxidation (Melanson et al., 2018). Morning or daytime light exposure thus far has indicated a positive or no significant effect on energy expenditure and substrate oxidation. At the same time, it is important to note that nighttime light exposure is most connected to negative physiological consequences of light pollution. One study looking into the effects of monochromatic blue light (465nm) 2h prior to sleep did not show any significant changes to energy metabolism during sleep but a significant decrease in energy expenditure in the subsequent morning after waking up (Kayaba et al., 2014), suggesting the potential influence of light exposure at night on energy metabolism. Yet no immediate response to light was observed during sleep despite the changes in the morning after. Thus, further studies need to be conducted to extend our understanding of light exposure on human energy metabolism during sleep.

1.8 Objective of the study

The aim of this study was to examine the effects of light in the evening on energy metabolism during sleep using spectrally different polychromatic LED and OLED light. Since OLED emit less blue light compared to the conventional LED light, setting a hypothesis that LED would negatively influence sleep by delaying sleep onset and reducing slow-wave activity, increase core body temperature inducing alertness, and reduce the decrease in energy expenditure during sleep. While reduced light, such as dim light, is suspected to show an opposite result to the LED condition, the spectral difference in OLED would mitigate some of the negative physiological responses mentioned above under LED, demonstrating metabolic responses resembling that of dim light.

Chapter 2: Materials and Methods

2.1 Participants

Ten healthy male participants (mean ± SE: 25.7 ± 0.65 years; BMI: 22.3 ± 0.65kg/m^2) were enrolled in a balanced cross-over study. All participants were non-smokers, medication-free, did not work night shifts or had not engaged in transmeridian travel at least one month prior to the experiment day. Participants reported no sleep disorders (Pittsburgh Sleep Quality Index < 6) and were classified as intermediate chronotypes assessed based on Morningness-Eveningness Questionnaire (MEQ) (Horne et al., 1976). The Ishihara Colorblindness Test was given to confirm normal color vision of the participants. The study was reviewed and approved by the ethics committee of the University of Tsukuba (Tai30-13; UMIN: 000042654), in compliance with the Declaration of Helsinki. All participant signed an informed consent before the experiment.

2.2 Experimental Protocol

Participants completed a 9-day experimental protocol including the 7-day at-home sleep/wake regulation period. Regularity was confirmed with a wrist actigraphy and self-reported sleep logs in which 7hr sleep was maintained with 30-minute acceptable range in fluctuations from the predetermined sleep time between 23:00 and 1:00. Three days prior to the experiment day, participants were restricted of caffeine and alcohol intake. Adaptation night was scheduled prior to the experiment days to familiarize themselves to sleeping in the metabolic chamber room.

The in-laboratory portion of the study was conducted at the sleep laboratory at the University of Tsukuba. Participants came to the laboratory six hours prior to their habitual bedtime (relative clock times normalized to a bedtime at 0:00). Body composition was measured using the bioimpedance method (BC-118E, TANITA, Tokyo, Japan) and all sensors were attached before entering the metabolic chamber. Upon entering the metabolic chamber, participants stayed in a sedentary position for 30 minutes to undergo dark adaptation. Light exposure to either 1000 lux of LED, OLED, or LED dim light (<10 lux) at eye level for continuous four hours prior to their habitual

sleep time. Participants maintained a sedentary position and were prohibited from using any electronic devices. Hourly questionnaire (Karolinska Sleepiness Scale; KSS) and task was given to assess sleepiness during light exposure. On day 2 immediately after waking up, participants answered a series of questions in the Oguri-Shirakawa-Azumi sleep inventory MA version (OSA-MA) which evaluate subjective sleep based on five factors including sleepiness after waking, initiation and maintenance of sleep, dreaming, how refreshed they feel, and sleep length. Energy metabolism, thermoregulation, as well as wakefulness were continuously measured for four hours after waking under regular room LED light (300 lux).

2.3 Light conditions

Light exposure was conducted using 4000K polychromatic white LED (OL291241, ODELIC Co., Ltd., Japan) and 4000K polychromatic white OLED (P09, Lumiotec Inc., Japan). The spectral power distribution was measured using an illuminance spectrophotometer (measured at 455nm for LED 1.89 x 10^{-2} W m-^{2} nm $^{-1}$ and OLED was 1.43 x 10^{-2} W m^{-2} nm^{-1}) (CL-500A, Konica Minolta Inc., Tokyo, Japan). Light panels (Organic Lighting Corporation, Yamagata, Japan) were directly set in front of the participants and distance was adjusted to achieve illuminance level of 1000 lux log photon flux: 14.97 $\log_{10}(cm^{-2}s^{-1})$) at eye level (with melanopic lux of 730 and 780 for LED and OLED respectively (Lucas et al., 2014)) using a lux meter before each experiment (CL-70F, Konica Minolta Inc., Tokyo, Japan). Luminance of the individual light sources were 3000 cd/m^2 and 300 cd/m^2 for LED and OLED respectively at 1000 lux. Spectral peaks were 545nm for OLED, 455nm for LED and dim light. Exposures to dim light on day 1 and morning room light on day 2 were conducted using a ceiling-mounted LED (Kitera 100, Aurora Daiichi, Aichi, Japan).

2.4 Measurements

2.4.1 Energy Metabolism

A whole room metabolic chamber was used to conduct continuous assessments of energy metabolism (Fuji Medical Science Co., Ltd., Chiba, Japan). The airtight chamber (2.00 x 3.45 x 2.10m; internal volume of 14.49m^2), was furnished with a mattress, desk, chair, and a toilet. The

airflow in the chamber was ventilated at a rate of 80L/min with temperature and humidity maintained at a constant 25.0 ± 0.5˚C and 55.0 ± 3.0%, respectively. Oxygen (O_2) and carbon diodide (CO_2) concentrations were measured by mass spectrometry (VG Prima δB, Thermo Electron Co., Winsford, UK) with precision of the mass spectrometry calculated from the standard deviation of measurements of a calibrated gas mixture (O_2 15%, CO_2 5%) which was <0.002% for both O_2 and CO_2. An improved algorithm for transient response was used to calculate the rates of hourly average of O_2 ($\dot{V}O_2$) consumption and CO_2 production ($\dot{V}CO$) (Tokuyama et al., 2009). Energy expenditure and macronutrient oxidation were calculated based on $\dot{V}O_2$, $\dot{V}CO_2$, and urinary nitrogen excretion (Ferrannini et al., 1988). Respiratory quotient (RQ) was determined as the ratio of $\dot{V}CO_2$ to $\dot{V}O_2$.

2.4.2 Sleep recordings

Participants were fitted with electrodes to record the polysomnogram (PSG) using a PSG-1100 (Nihon Kohden, Tokyo, Japan). Electroencephalograms (EEG) was recorded using electrodes that were attached at F3/M2, F4/M1, C3/M2, C4/M1, O1/M2, and O2/M1, along with electrooculogram (EOG) and electromyogram (EMG). Visual scoring based on the standard criteria was conducted by a registered polysomnographic technologist (Berry et al., 2018). EEG data derived from C3/M2 was used to conduct fast Fourier transformation (FFT) with a window length of 5-s to obtain a 0.2Hz resolution (Park et al., 2017). Spectral results were used to calculate the delta power density during non-rapid eye movement sleep in the frequency range from 0.75-4.00Hz for each 30-s epoch of sleep.

2.4.3 Thermometry

Core body temperature was measured using a CorTemp sensor and a data recorder (CorTemp, HQ Inc., Palmetto, FL, USA). The sensor, accurate to ± 0.1˚C, was contained in a silicone covered, single-use ingestible pill, which was calibrated every time before use. Data was recorded every 30s continuously during the experimental days and the results were reported as an hourly average.

Skin temperature was recorded using a Thermistor probes (ITP082-24, Nikkiso-Thermo Co., Tokyo, Japan) connected to a data logger (N543, Nikkiso-Thermo Co.). Sensors were attached at four

proximal points (infraclavicular area, midthigh on the right musculus rectus femoris, 1 cm above the navel on the stomach, and forehead) and four distal points (back of right and left hands, middle of right and left foot instep). Mean proximal temperature was calculated with the following equation; (forehead x 0.093) + (thigh x 0.347) + (infraclavicular area x 0.266) + (stomach x 0.294). Mean distal temperature was calculated as mean of both hands and feet. Distal-proximal gradient (DPG) was the difference between the distal and proximal skin temperatures (Kräuchi et al., 2000). Data was recorded continuously for during the experimental days with results reported as an hourly average.

2.4.4 Urinary sulfatoxymelatonin (aMT6s)

Collection of urine sample began 4h prior to sleep to 4h after waking up while the participants were in the metabolic chamber. The combined total volume of urine during the experimental days were measured and stored at -20˚C until assay. Urinary aMT6s was assayed from the sampled urine by fluorometric high-pressure liquid chromatography (Minami et al., 2009) comprised of an LC-20AD pump system (Shimadzu, Kyoto, Japan), equipped with RF-10-A spectrofluorometer (Shimadzu, Kyoto, Japan), Inertsil ODS-3 analytical column (5020-01732 GL Sciences, Tokyo, Japan), column oven kept at 40˚C (GL Science, Tokyo Japan), and LCsolution (Version 1.22 SP1 software, Shimadzu, Kyoto, Japan). All melatonin metabolites were assayed using indole-3-acetamide as the internal standard and normalized to urinary creatinine levels to control for variations in the urine concentration (Bonsnes et al., 1945).

2.5 Statistical Analysis

All data are presented as mean ± SE. Specific statistical tests are indicated in the text. Two-way repeated measures ANOVA for time course analysis and one-way repeated measures ANOVA for the mean values with post hoc analysis using Bonferroni adjustment were applied. The effect size was determined using generalized eta-squared (0.01, small; 0.06, medium; 0.138, large) (Bakeman et al., 2005; Richardson et al., 2011). Effect sizes comparing two means between the light conditions were expressed using Cohen's *d* (0.2, small; 0.5, medium; 0.8, large). Semiparametric regression analysis was used to analyze energy metabolism by sleep stages (Kayaba et al., 2017). Association

analysis was conducted using Pearson's correlation analysis. All statistical analysis were conducted using R studio (version: 1.2.1335, R Consortium, https://www.r-consortium.org).

Chapter 3: Results

3.1 Sleep

The overall sleep architecture did not differ significantly among the three light conditions (Table 1). To investigate the effects of light exposure on sleep homeostasis, EEG delta power (0.5-4 Hz) during slow-wave sleep was analyzed. Time course of the delta power revealed no significant difference in the interaction between time and condition ($p=0.125$, $\eta^2_G=0.06$) (Fig. 5). Delta power density, expressed as the percentage of delta power over the total power (0.75-30.0 Hz) during slow-wave sleep did not differ significantly among the three light conditions ($p=0.425$, $\eta^2_G=0.05$) (Fig. 5).

Continuity of sleep was assessed based on the frequency of transition between the sleep stages. This was counted every time there was a change in sleep stage. Frequency of the change into NREM1, NREM2, SWS, REM, or wake did not differ significantly among the light conditions (Table 2). Sleep fragmentation was then assessed based on the duration of slow-wave sleep episodes. Although dim light and OLED showed a slightly longer episode duration with 3.46 ± 0.46 min and 3.40 ± 0.46 min respectively, and LED with a shorter 2.98 ± 0.48 min.

Participants subjective sleepiness during wake periods were assessed using Karolinska Sleepiness Scale in which they rated their sleepiness based on a 9-point scale from 1 being extremely alert to 9 being extremely sleepy. The hourly questionnaire during light exposure and after awakening on day 2 did not demonstrate any significant difference among the conditions during the nighttime ($p=0.374$, $\eta^2_G=0.009$) and after waking on day 2 ($p=0.557$, $\eta^2_G=0.004$) (Fig 5). Subjective sleep, assessed from Oguri-Shirakawa-Azumi sleep inventory middle-age version, indicated no significant difference in sleepiness after waking up ($p=0.922$, $\eta^2_G=0.001$), initiation of sleep ($p=0.712$, $\eta^2_G=0.02$), frequency in dreaming ($p=0.916$, $\eta^2_G=0.007$), feeling of refresh ($p=0.278$, $\eta^2_G=0.09$), or on subjective feeling on the length of sleep upon awakening ($p=0.537$, $\eta^2_G=0.03$) (Table 3).

3.2 Energy metabolism

Time course of energy expenditure, respiratory quotient (RQ), fat oxidation, and carbohydrate oxidation are shown in figure 6. Two-way repeated measures ANOVA on hourly energy expenditure, RQ, fat oxidation, and the carbohydrate oxidation revealed any significant main effect in condition or on interaction (Fig 6). The mean RQ nadir time was later under the light conditions which were 3.3 ± 0.4 hrs, 4.1 ± 0.6 hrs, and 4.0 ± 0.4 hrs after lights off for dim, LED, and OLED respectively, but the differences were not significant ($p=0.5$, $\eta^2_G=0.05$).

The average energy expenditure, respiratory quotient, and fat oxidation were further analyzed separately based on sleep and wake periods (Fig. 7, Table 4). During sleep, there was a significant difference in average energy expenditure ($p=0.003$, $\eta^2_G=0.02$) with a post hoc comparison showing lower value under OLED compared with dim light ($p<0.001$, $d=0.3$). The average RQ was significantly different ($p=0.029$, $\eta^2_G=0.03$) with post comparison indicating higher value under LED compared with OLED ($p=0.016$, $d=0.47$). This was consistent with the significant decrease in fat oxidation ($p=0.003$, $\eta^2_G=0.06$) with post hoc comparison revealing significantly higher value under LED compared with OLED ($p=0.001$, $d=0.60$) and dim light ($p=0.003$, $d=0.53$). These effects persisted to the next morning after waking. The average energy expenditure on day 2 was significantly different ($p=0.002$, $\eta^2_G=0.03$) with lower value under OLED compared with dim ($p=0.001$, $d=0.43$) and lower value under LED compared with dim ($p=0.047$, $d=0.21$). The average RQ remained high after waking ($p=0.03$, $\eta^2_G=0.03$) with a higher value under LED compared with dim light ($p=0.024$, $d=0.37$). Fat oxidation was significantly different ($p=0.005$, $\eta^2_G=0.05$) with post hoc comparison showing lower value under LED compared with dim light ($p=0.003$, $d=0.53$). Carbohydrate ($p=0.163$, $\eta^2_G=0.01$) and protein oxidation ($p=0.307$, $\eta^2_G=0.09$) were unaffected by the light conditions.

Energy metabolism adjusted by sleep stages showed a pattern that energy expenditure, RQ and carbohydrate oxidation decrease with the progression of sleep stages (Fig. 8). Although the results were not significant, consistent with the mean values during sleep, RQ under LED condition showed higher values while fat oxidation was suppressed under all sleep stages.

3.3 Thermoregulation

Time course analysis on core body temperature revealed no significant effect of light condition ($p=0.162$, $\eta^2_G=0.10$) but a significant interaction between condition and time ($p=0.016$, $\eta^2_G=0.03$) (Fig. 9). Post hoc analysis showed a significant increase in the body temperature under LED compared with dim light 2 hours before sleep and significant decrease in temperature under OLED compared with dim light during sleep. Average body temperature during sleep was significantly lower ($p<0.001$, $\eta^2_G=0.07$) with post hoc revealing significant decrease in OLED compared with dim ($p=0.001$, $d=0.64$) and LED during sleep ($p=0.001$, $d=0.44$) and after waking up for dim ($p<0.001$, $d=0.71$) and LED ($p<0.001$, $d=0.45$) (Fig. 10a, 10b, Table 5).

Skin temperature was assessed from proximal and distal regions by attaching eight sensors throughout the body (Fig. 9). Two-way repeated measures ANOVA on the time course of proximal temperature revealed no significant effect of condition ($p=0.327$, $\eta^2_G=0.02$), but a significance in the interaction between condition and time ($p=0.009$, $\eta^2_G=0.09$) with a decrease in OLED compared with dim light after waking at 10:00. Proximal temperature assessed at the forehead showed a significant increase in OLED compared with LED during and after sleep, however no significant differences in temperature were observed in other locations. There was no significant main effect of light condition or on the interaction between condition and time observed from distal temperature or the distal proximal gradient (DPG).

The average temperature during sleep was then assessed using a one-way repeated measures ANOVA on proximal and distal temperatures and on the DPG (Fig. 10, Table 5). During sleep, the proximal temperature was significantly different among the conditions ($p=0.0004$, $\eta^2_G=0.010$) with significant post hoc between LED and OLED ($p=0.004$, $d=0.38$), and LED and dim light ($p=0.002$, $d=0.34$). A greater widening of the DPG ($p=0.001$, $\eta^2_G=0.05$) was observed in both dim light ($p=0.02$, $d=0.27$) and OLED ($p<0.001$, $d=0.50$) compared with LED after post hoc analysis. The distal temperature did not differ significantly among the light conditions.

Body temperature positively correlated with energy expenditure during the sleep period ($r^2=0.22$, $p<0.001$) and wake period ($r^2=0.25$, $p<0.001$). The decline in energy expenditure was correlated with a decrease in body temperature for all light conditions (Fig. 12).

3.4 Urinary aMT6s

Total urinary excretion of 6-sulfatoxymelatonin (aMT6s) did not differ between the light conditions ($p=0.923$, $\eta^2_G=0.001$) (Fig. 13). Urinary melatonin metabolites and energy metabolism were then further analyzed for their correlation. There was no correlation between aMT6s and RQ in any of the light conditions; dim light ($p=0.52$), OLED ($p=0.42$), and LED ($p=0.41$). A significant positive correlation between urinary aMT6s and fat oxidation was observed under OLED ($r^2=0.46$, $p=0.032$). There was no correlation under dim light ($r^2=0.36$, $p=0.068$) or LED ($p=0.96$).

Chapter 4: Discussion

4.1 Significance of the study

Evening exposure to polychromatic light altered the energy metabolism and core body temperature during sleep while showing little effect on the sleep architecture, suggesting that the influence of light on energy metabolism and thermoregulation observed in the present study is possibly affected by regulatory systems unrelated to those of sleep. The effect on metabolism continued until after waking the subsequent morning.

4.2 Sleep was unaffected by light exposure

Wavelength dependency of light on sleep and the circadian rhythm is such that exposure to shorter wavelength of light in the evening suppress melatonin and increase sleep latency (Münch et al., 2006). Exposure to monochromatic blue light (460nm) compared to green light (550nm) reduces slow wave-activity (Münch et al., 2006), and polychromatic, blue-enriched light reduces frontal NREM slow-wave activity during the first cycle of sleep (Chellappa et al., 2013). Arousal promoting responses to light has also been studied in nocturnal mice such that blue light (470nm) causes arousal by delaying sleep onset whereas green light (530nm) produces a sleep-inducing behavior, possibly through different pathways from ipRGCs to suprachiasmatic nucleus (SCN) or to ventrolateral preoptic area (VLPO) (Pilorz et al., 2016). In the present study, however, differences in homeostatic sleep pressure, assessed from slow-wave activity, were not observed from a one-night exposure to spectrally different light. Additionally, subjective sleep and sleepiness evaluated based on KSS and OSA questionnaires did not differ significantly among the light conditions. The results in the present study did not show any significant results on sleep in response to evening light was consistent with findings from a previous study comparing the effects of OLED and LED on sleep (Park et al., 2020). The contradictory outcomes on sleep may be due to the methods of administering light among the studies. Direct, high-intensity light utilizing a customized ganzfeld dome or goggles is often used in light exposure experiments (Brainard et al., 2001; Zeitzer et al., 2011). In the present study, as well as in the previous study by Park

and colleagues (Park et al., 2020; Jo et al., 2021), light exposure was conducted using ambient light placed above or in front of the participant's angle of gaze. Thus, the precise amount of light reaching the retina at the cornea level remains to be an approximation. Nevertheless, it should be noted that ambient lighting more closely resembles our daily light exposure.

4.3 Alerting effect of LED exposure before sleep

The alerting effect of light before sleep is reflected on EEG activity (Chang et al., 2015) but also on thermoregulatory parameters such that exposure to bright light prior to sleep significantly increases core body temperature compared with dim light (Cajochen et al., 1992; Dijk et al., 1991). Likewise, evening exposure to monochromatic blue light significantly increases the core body temperature compared with monochromatic green and dim light (Münch et al., 2006; Cajochen et al., 2005). The significant increase in core body temperature under the LED condition two hours before sleep in the present study also supports the alerting effect of high content of blue light evaluated in previous studies.

4.4 Reduction in core body temperature in relation to energy expenditure

Core body temperature is known to decrease before and during sleep, reflecting the suppression of heat production and enhancement of heat loss from distal regions of the body (Kräuchi et al., 2001). Heat dissipation from the core to the periphery is described as DPG, and its increase is associated with sleep propensity (Kräuchi et al., 1999). In the present study, despite the significant decrease in core body temperature during sleep in OLED compared with dim light, DPG and the proximal/distal temperatures did not differ significantly between the two conditions. This is in line with a previous study reporting the inconsistency in core body temperature and heat dissipation following evening exposure to monochromatic blue, green, and dim light (Cajochen et al., 2005). Therefore, heat dissipation alone is insufficient to explain the drop in the core body temperature during sleep exhibited in the present study in the OLED condition.

Heat production in the form of energy expenditure was also significantly lower in OLED compared with dim light. This attenuation in energy expenditure, as well as core body temperature, may

be the result of the Q_{10} effect, measuring the change in a biological process due to a change in temperature, which downregulates metabolism by decreasing body temperature. A previous study on patients with pathological conditions showed that a 1°C increase in body temperature is associated with an approximate 13% increase in the metabolic rate (Du Bois et al., 1921). The Q_{10} of biological reactions mainly ranges between 2.0 and 3.0 with a 7%-12% increase in the rate of a chemical reaction from a 1°C rise in temperature (Hochachka et al., 1984). Because the regression analysis in the present study showed a 10.4% change in energy metabolism due to an increase of 1°C, the decrease in energy expenditure in OLED may be explained by the Q_{10} effect. Body temperature, however, also varies with energy expended in the form of heat production. The decrease in temperature and energy expenditure observed under OLED may be linked with one another but causal effect of the two factors remains elusive.

4.5 Possible underlying mechanism on light and thermoregulation

The acute effect of body temperature in response to light exposure have previously been confirmed in mice. Nocturnal mice respond to light with a suppression in locomotion and an immediate drop in body temperature (Morin et al., 2013). It has also been reported that light detected by the ipRGCs send direct projections to brain areas mediating acute effect on body temperature, independent from that to SCN, which have been suspected to surround the preoptic area, important in thermoregulation (Rupp et al., 2019). It is plausible that the ipRGC subtypes that express Brn3b transcription factor (M2-M6) responsible in the non-SCN projection, may have responded to a particular characteristic in wavelength of OLED to decrease the temperature during sleep without affecting sleep itself. However, since dim light had not shown any significant reduction in body temperature compared with the light exposure conditions, characteristics of OLED other than wavelength may be an important contributor in decreasing body temperature. Further studies on how light, especially OLED affects acute responses to body temperature need to be conducted.

4.6 Light exposure and metabolic flexibility

The ability to select fuel in response to alterations in the nutritional and physiological states is referred to as metabolic flexibility and is often measured as the change in RQ of whole-body energy metabolism (Kelley et al., 1999). RQ, measuring the ratio of carbon dioxide produced and oxygen consumed, is an indicative measurement of substrate utilization where high RQ signifies carbohydrate oxidation while low RQ reflects fat oxidation (Schutz et al., 1995). During the fasting state, such as during sleep, energy metabolism becomes reliant on fat oxidation and maintains a low RQ (Galgani, et al., 2008). In the present study, evening exposure to LED light resulted in a significantly higher RQ compared with exposure to the OLED light, and a significant decrease in fat oxidation during sleep. The difference in RQ during sleep suggests that exposure to different light spectra at night affects substrate oxidation, providing a plausible link between light exposure at night and weight gain (Wyse et al., 2011).

Previous studies have shown that the inability to switch to fat oxidation during sleep is associated with an increased risk of obesity (Mynatt et al., 2019). Small fat to carbohydrate oxidation ratio has been implicated to be associated with obesity and diabetes. A longitudinal study investigating the 24h RQ in nondiabetic Pima Indians showed that individuals with higher RQ and a low ratio of fat to carbohydrate oxidation were at higher risk of weight gain compared to those with lower RQ (Zurlo et al., 1990). Other studies have also shown a significant correlation between higher RQ and body weight (Seidell et al., 1992, Suter et al., 1992) or type 2 diabetes (Pujia et al., 2019). Although it is unknown whether improving RQ will contribute to the prevention of metabolic syndrome or diabetes, animal models have shown effectiveness in preventing diabetes and weight loss by improving free fatty acids and RQ (Etgen et al., 2000). The low RQ value and high fat oxidation observed under the OLED, which was comparable to the dim light condition, suggests its ability to adapt physiologically despite the exposure to evening light at night.

4.7 Role of melatonin on energy metabolism

The specific factors that contribute to the alteration of substrate oxidation by light exposure remain to be identified. One of the main key factors transmitting photic stimulation to regulate energy

metabolism is the hormone melatonin, the secretion of which is suppressed by light with an optimal sensitivity to short wavelengths between 446 and 477 nm (Brainard et al., 2001). Melatonin, produced in the pineal gland, binds to melatonin receptors which are expressed throughout the body, including pancreatic islets, adipose tissue, skeletal muscle, and liver, thus entraining the downstream circadian rhythm (Ha et al., 2006; Nagorny et al., 2012). In the present study, concentration of aMT6s was assessed, a major urinary metabolite of melatonin, which is strongly correlated with the serum melatonin concentration (Nowake et al., 1987). The total excretion of aMT6s, however, did not differ among the light conditions. This is partly due to the poor time resolution of the collected urinary samples as they reflect the total combined amount of aMT6s from day 1 to day 2 of the experimental days in the metabolic chamber. For this reason, temporal changes in the concentration of melatonin metabolites were not identified.

Additionally, because melatonin has a large inter-individual variability (Burgess et al., 2008), we further analyzed the correlation between aMT6s and metabolic parameters. The results in the present study indicated that aMT6s excretion was marginally (p=0.068) and significantly (p=0.032) correlated with fat oxidation in the dim and OLED conditions, respectively. This finding was consistent with that of a previous study showing an inverse correlation between RQ and melatonin (Tapia 2018). Interestingly, the tendency toward a positive correlation between aMT6s excretion and fat oxidation was not observed in the LED condition (p=0.96). This suggests that the role of melatonin to stimulate lipolysis in intramuscular adipocytes (Yang et al., 2017, Li et al., 2019) may not be preserved under exposure to LED, but retained under exposure to OLED, possibly due to the reduction in the blue light spectrum. However, since OLED showed a stronger positive correlation compared to dim light despite the increase in intensity and short wavelength of blue content, spectral composition alone seems to be insufficient to explicate these results. Temporal changes in melatonin concentration need to be assessed to further understand its relation to energy metabolism during sleep.

Additionally, although the spectral peak occurred at 454nm for LED, there is still limitation in using blue light to excite melanopsin with a maximum sensitivity at 480nm (Berson et al., 2002). Considering that the melanopic lux between LED and OLED in the present study were 730 and 780 lux respectively, the effect of the spectral composition of LED peaking at 454nm of blue light did not reflect

clearly on the melanopic functions. In addition, since the non-image forming responses to light is partially compensated by rods and cones (Panda et al., 2002), melanopic responses alone may not be sufficient to explicate the effects of spectral differences between LED and OLED.

4.8 Metabolic responses in relation to sleep stages

The relationship between RQ and sleep stages showed a non-significant tendency for a higher RQ under the LED condition in all stages of NREM sleep. A previous study on fragmented sleep on energy metabolism has shown that sleep fragmentation led to a decrease in TST, SWS, and REM and elevated sleepiness, RQ, and carbohydrate oxidation (Hursel et al., 2011). SWS and SWA specifically have also been correlated with endocrine parameters such that the disruptions in SWS lead to a reduction in the adequate response to glucose, reduction in insulin sensitivity, which in turn is associated with the increase in the risk of diabetes (Tasali et al., 2007). In the present study, stage shifts throughout the night and SWS episode duration assessing fragmentation in SWS did not differ significantly between the conditions. However, the elevated RQ exhibited in all stages of NREM sleep under the LED condition may be indicative of the sleep disruption that was not necessarily reflected in the current EEG activity.

4.9 Limitations of the study

In the present study, measurements of energy metabolism and thermoregulation were conducted for only one night, thereby limiting our understanding of the overall metabolic changes throughout the day. Considering that the physiological impact of light varies with the timing of the exposure (St. Hilaire et al., 2012), it is likely that daytime metabolism is altered depending on the intensity, duration, and wavelength of light. Additionally, although our experiment was not designed to account for the circadian changes caused by light exposure, a preliminary study showed that maintaining a modified constant posture in dim light (< 10 lux) for 8 h prior to sleep moved the core body temperature nadir time to either 30 min before or at sleep onset (unpublished data). Thus, it is important to note whether dim light is indeed an ideal control to compare with the other light exposure conditions as it has its own characteristic to possibly shift body temperature to an earlier time.

Additionally, future studies involving light exposure must take into consideration the participants' age and sex, as these factors may also impact energy metabolism (Zhang et al., 2020; Roberts et al., 2006).

4.10 Future directions

The present study is one of the first to show that evening light exposure affects metabolism by selectively utilizing substrates during sleep and the subsequent morning after waking. The contrasting metabolic outcomes observed in the LED and OLED conditions may indicate differences in the spectral composition of light in which the short wavelength of blue light negatively affects energy metabolism by increasing the RQ and decreasing fat oxidation during sleep and after waking. Because the spectral composition and melanopic lux between LED and OLED did not differ greatly, it is important to note that characteristics of light, apart from wavelength, such as the glare, luminance, and frequency of fluctuation (Inger et al., 2014), may play an additional role in human physiology. Nevertheless, these findings suggest that OLED may be a viable alternative source of light at night.

Chapter 5: Figures and Legends

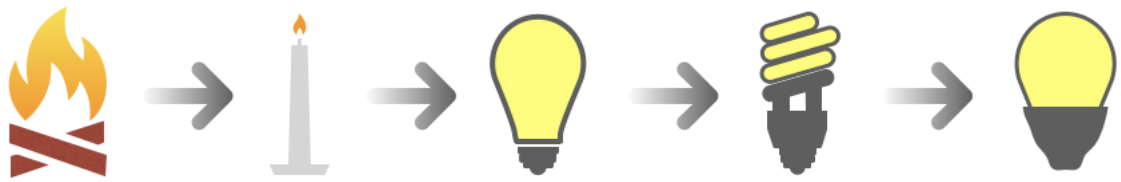

Figure 1. Evolution of light from the start of civilization to modern days
Light evolved from fire to candle usage (3000 BC) to the invention of fluorescent (1847), incandescent (1879), and LED (1962). First compact fluorescent lamp was not commercialized until 1981. OLED molecules was introduced in 1987, white LEDs in 1995, white OLED in 1995 (Chitnis et al., 2016; Kido et al., 1995).

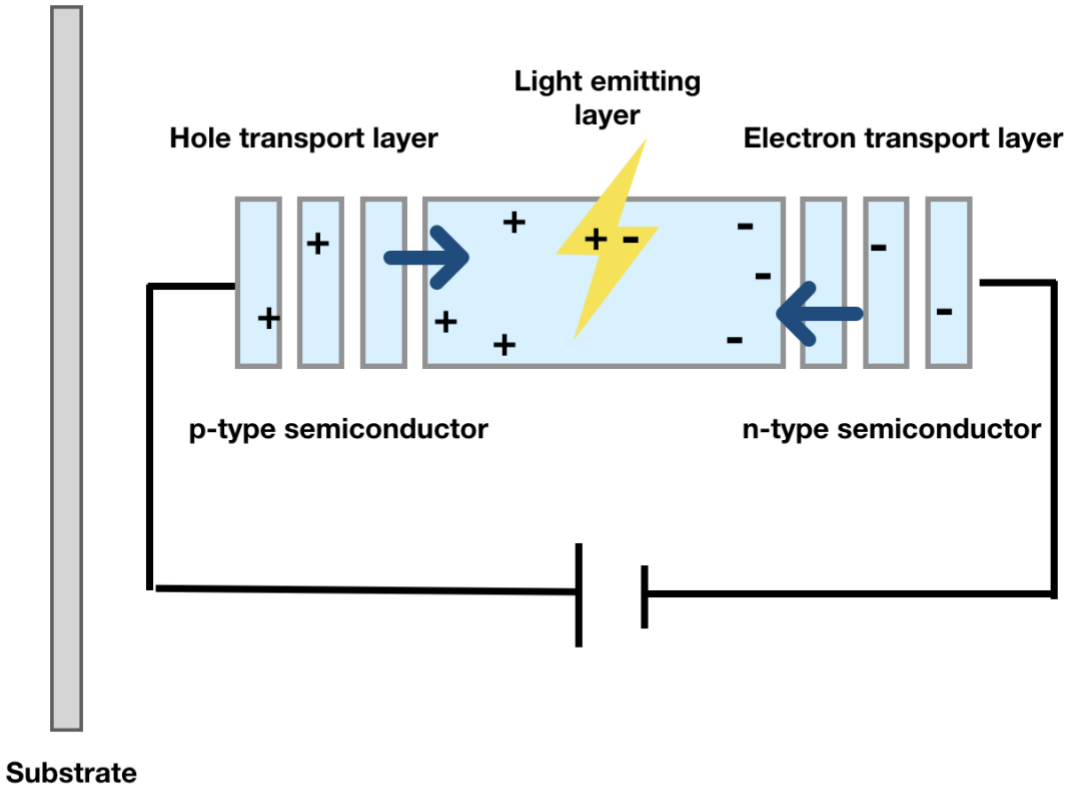

Figure 2 Principles of LED and OLED light
LED and OLED composed in sandwiched layers between the anode and cathode. Light is emitted at the light-emitting layer, consisted either of organic or inorganic compound, and is excited by the energy of electrons from cathode and holes from the anode.

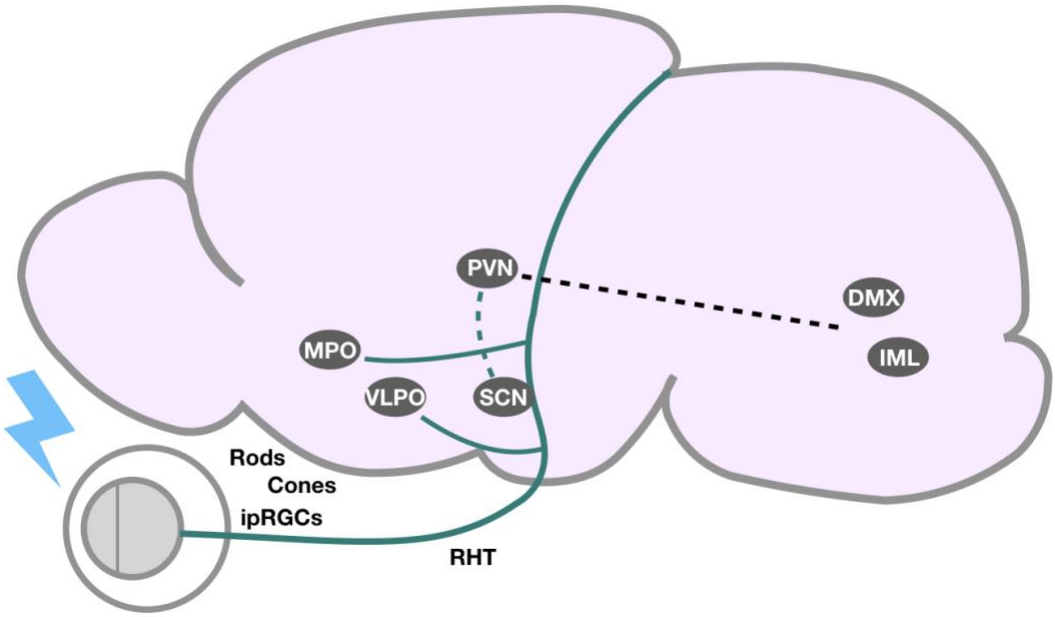

Figure 3 Photic input from ipRGC and its projections confirmed in mice brain
Light detected by the ipRGC travel through retinohypothalamic tract (RHT) inducing direct input including the suprachiasmatic nucleus (SCN), ventrolateral preoptic nucleus (VLPO), medial preoptic area (MPO), paraventricular nucleus (PVN), intermediolateral column of the spinal cord (IML), and dorsal motor nucleus of the vagus (DMX). (Figure modified from Fleury et al., 2020).

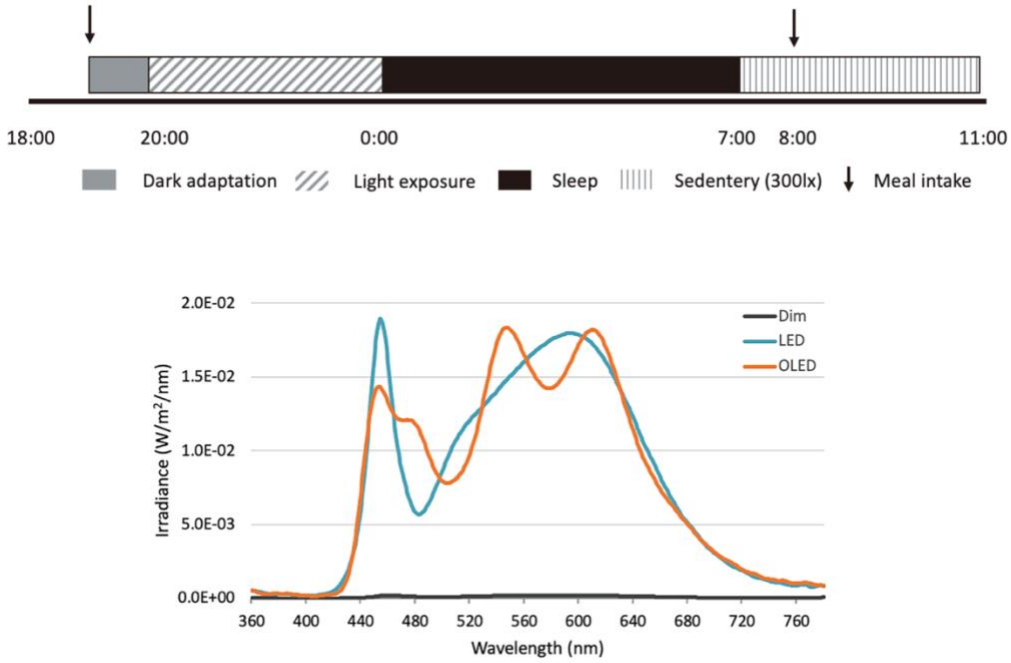

Figure 4 Study protocol and spectral distribution of each light conditions
(Top) Exposure to either LED (1000 lux), OLED (1000 lux) or dim (< 10 lux) light were conducted at eye level, 4 hours prior to sleep. Time of day indicated as relative hours with lights off at 0:00 and lights on at 7:00. (Bottom) Spectral distribution and intensity of each wavelength is expressed as irradiance for dim light, LED, and OLED light.

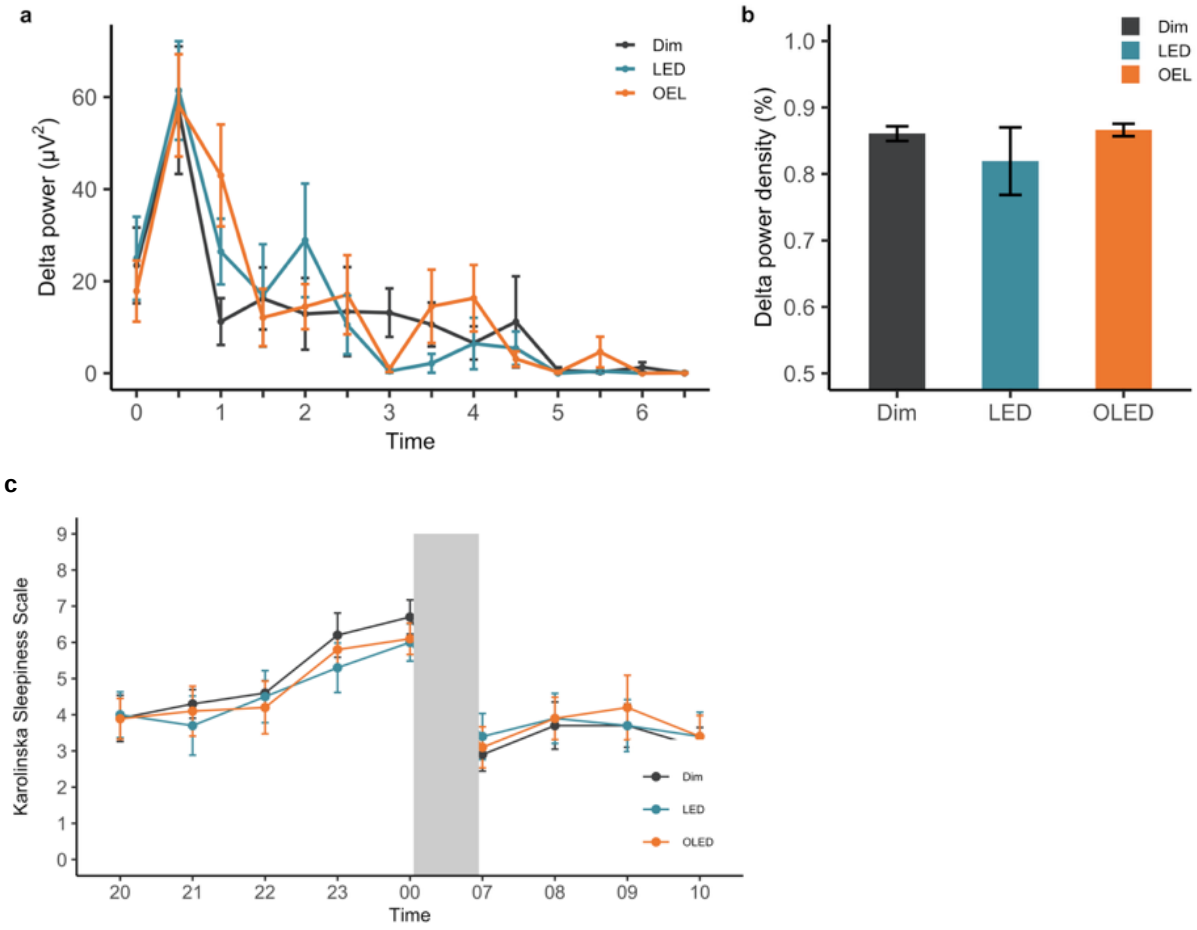

Figure 5 Delta power during slow-wave sleep and subjective sleep
(a) Time course of delta power during SWS under dim (black), LED (blue), and OLED (orange). (b) Delta power density expressed as the percentage of delta power over the total power between 0.75Hz to 30.0Hz during SWS under dim, LED, and OLED. (c) Subjective sleep scores assessed from Karolinska Sleepiness Scale (KSS). Grey bar indicate time asleep.

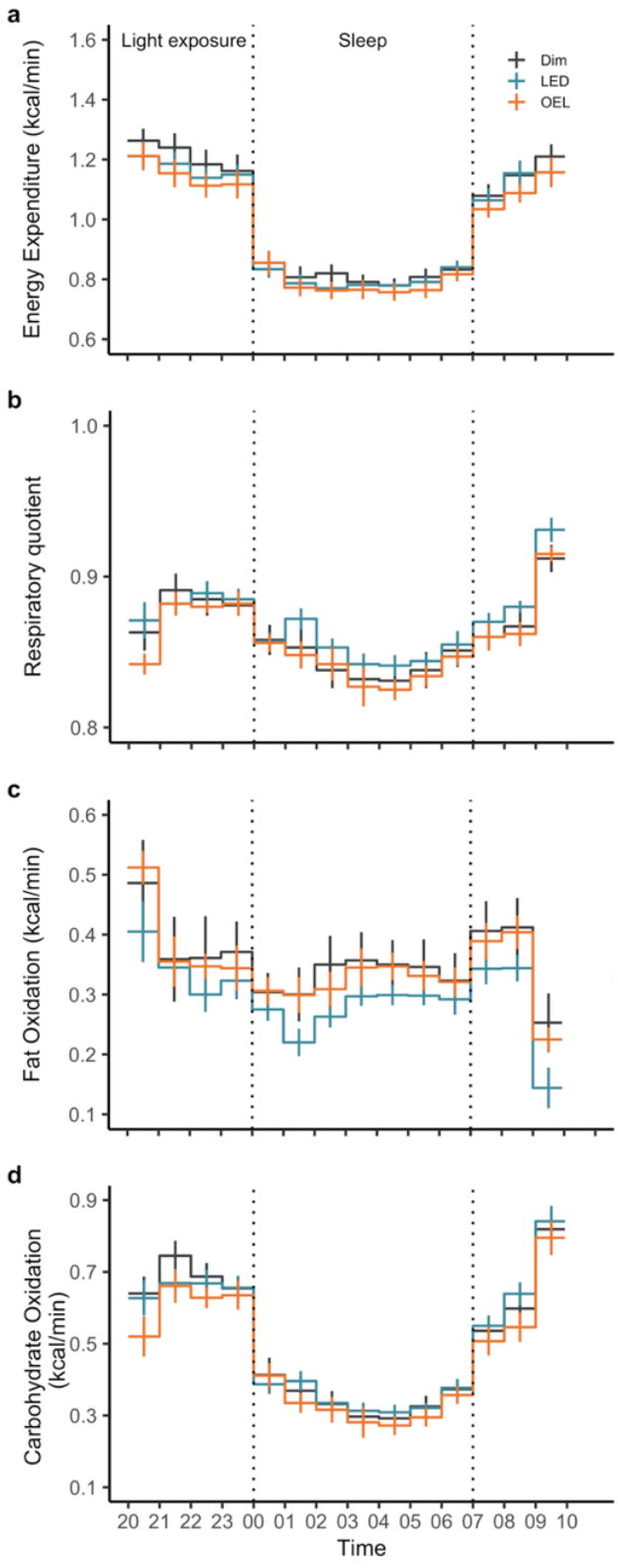

Figure 6 Time course of energy metabolism
Time course of (a) energy expenditure, (b) respiratory quotient, (c) fat oxidation, (d) carbohydrate oxidation for dim (black), LED (blue), and OLED (orange) conditions.

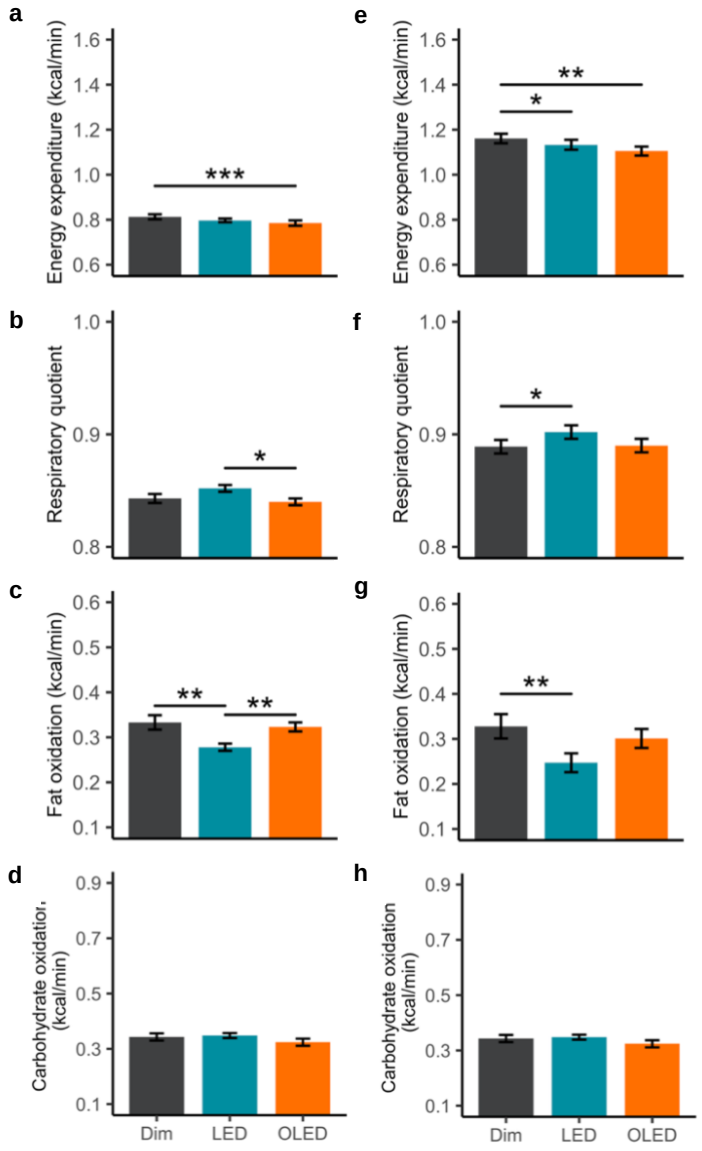

Figure 7 Average values of energy metabolism
(a) energy expenditure, (b) respiratory quotient, (c) fat oxidation, (d) carbohydrate oxidation during sleep, (e)energy expenditure, (f) respiratory quotient, (g) fat oxidation, (h) carbohydrate oxidation during wake on day 2. Significance indicated as one-way repeated measures ANOVA with Bonferroni's adjustment, *p<0.05, **p<0.01, ***p<0.001.

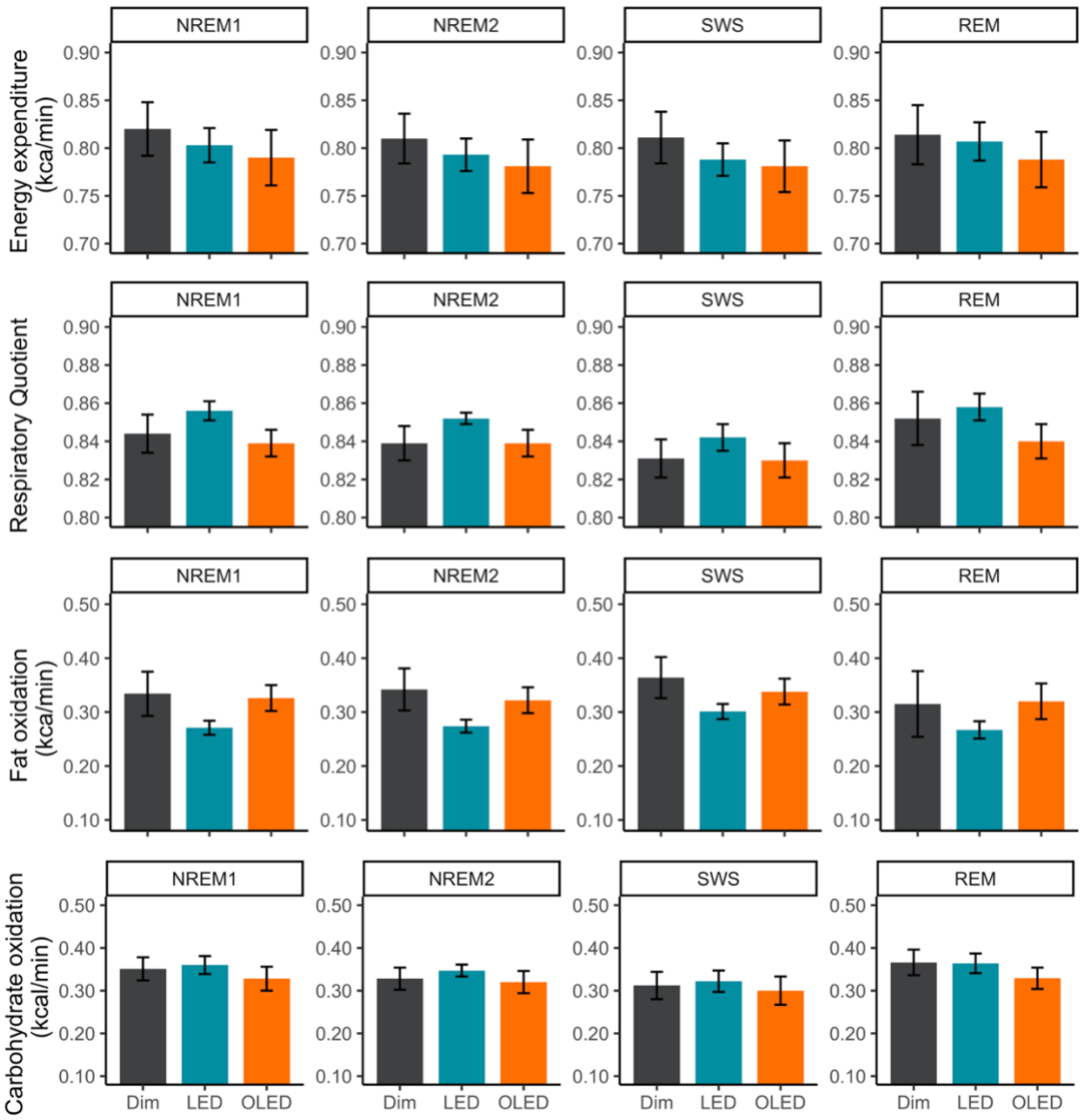

Figure 8 Energy metabolism parameters adjusted by sleep stages
Each of the parameters of energy metabolism are plotted based on sleep stages using semiparametric analysis.

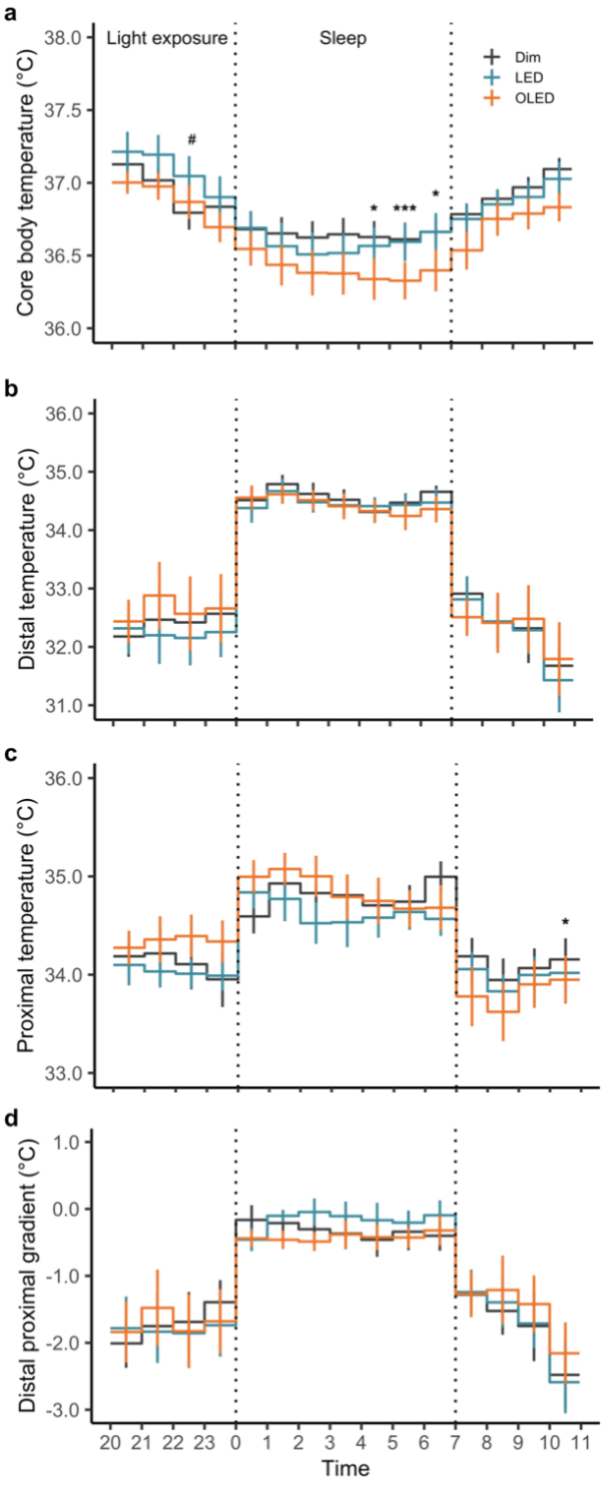

Figure 9 Time course of thermoregulation
Thermoregulation measured from (a) core body temperature, (b) distal temperature, (c) proximal temperature, (d) distal proximal gradient. Two way-repeated measures ANOVA with post-hoc pairwise comparison with Bonferroni's adjustment; *p<0.05, **p<0.01, ***p<0.001 between OLED and dim light, #p<0.05 between LED and dim light.

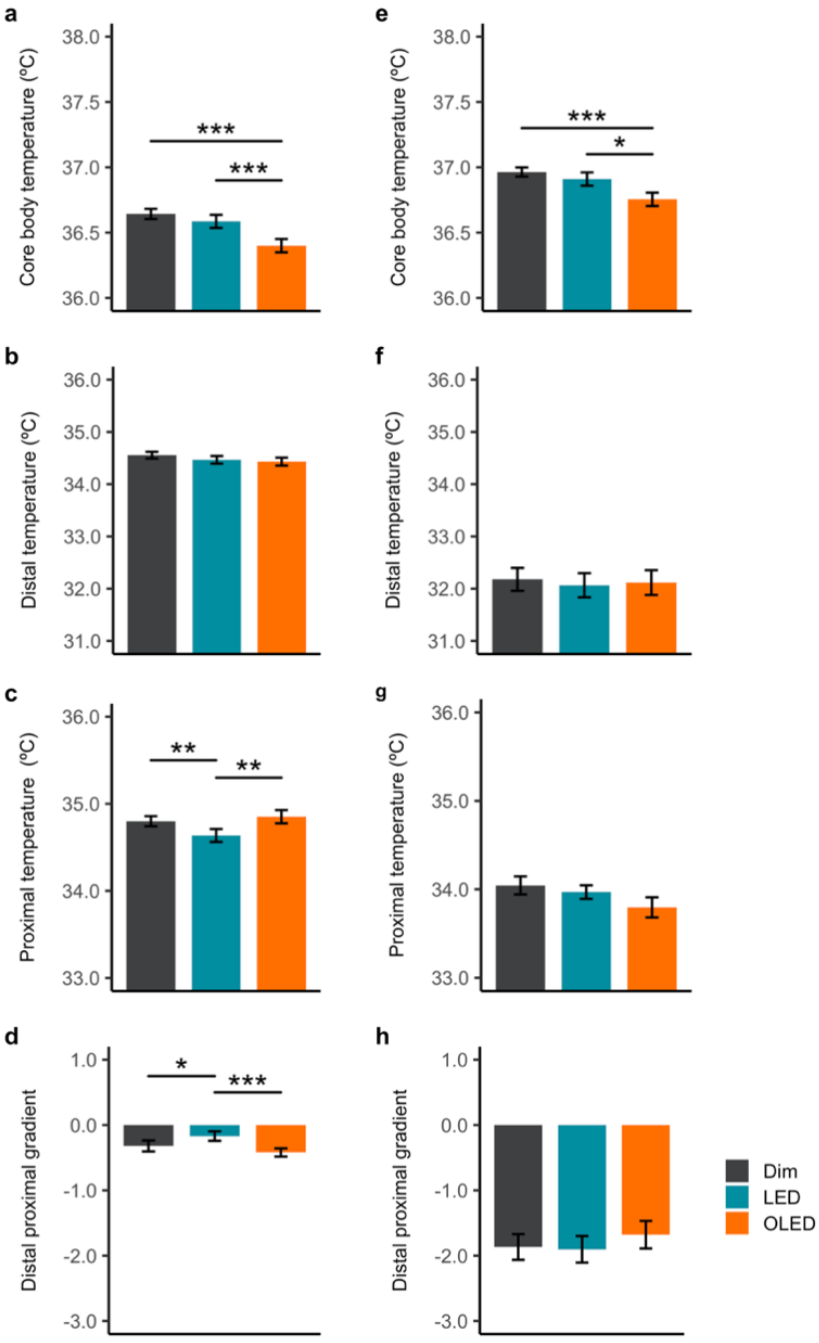

Figure 10 Average values of thermoregulatory measures
(a) core body temperature, (b) distal temperature, (c) proximal temperature, (d) distal-proximal gradient during sleep and (e) core body temperature, (f) distal temperature, (g) proximal temperature, (h) distal-proximal gradient during wake on day 2. P-values are indicated as *p<0.05, **p<0.01, ***p<0.001 for one-way repeated measure ANOVA with Bonferroni corrections.

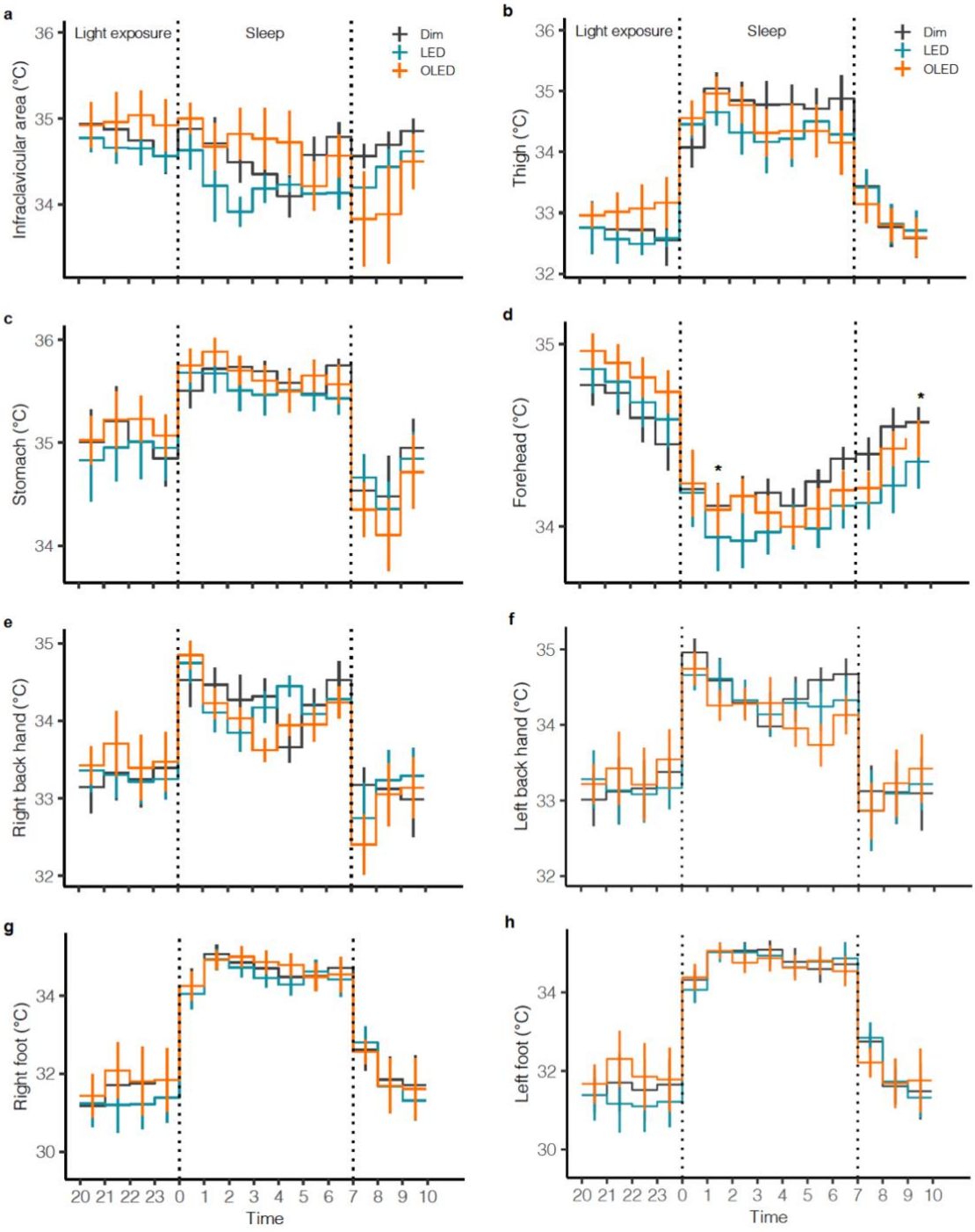

Figure 11 Time course of temperature changes in 8 locations
(a) infraclavicular, (b) thigh, (c) stomach, (d) forehead, (e) right back hand, (f) left back hand (g) right and (h) left feet measured by n=8 participants. Dim (black), LED (blue), and OLED (orange) during time in metabolic chamber. P-values indicate two-way repeated measures ANOVA *p<0.05 between LED and OLED.

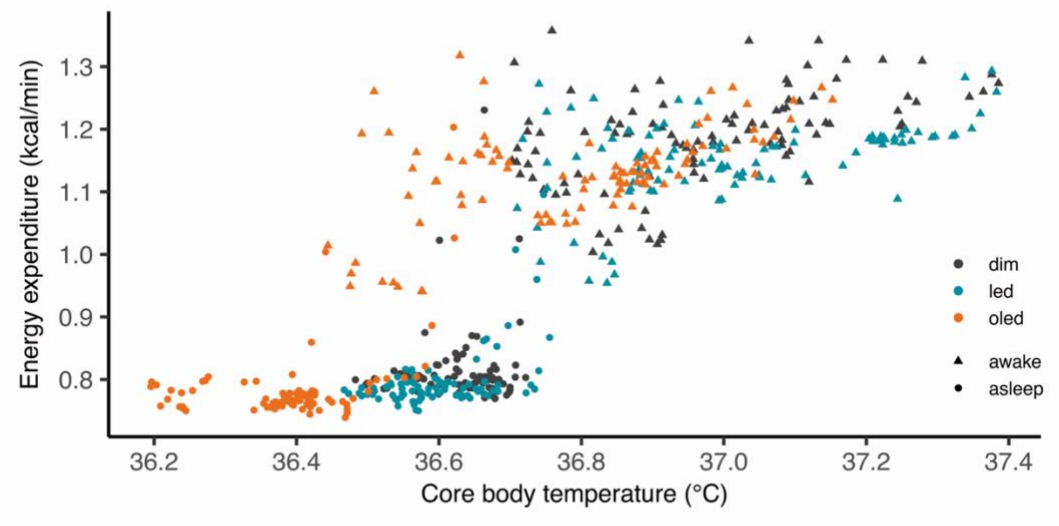

Figure 12 Relationship between energy expenditure and core body temperature
Correlation is plotted as 5-minute mean during sleep (circle) and wake (triangles) for dim (black), LED (blue), OLED (orange).

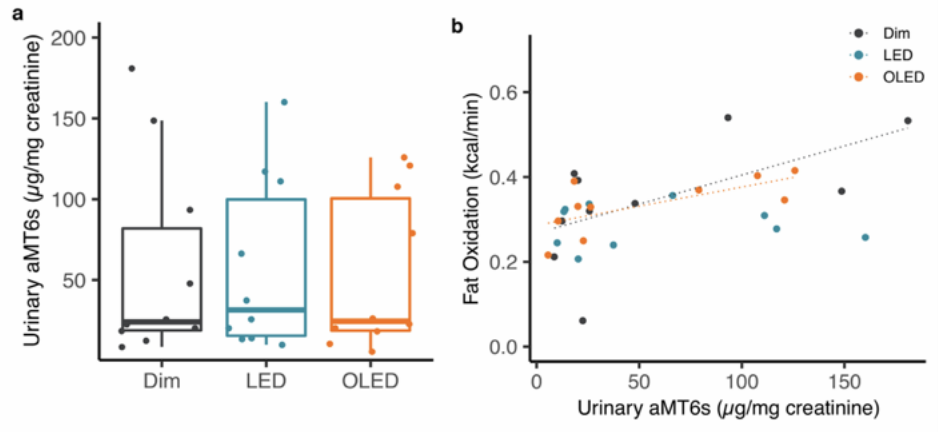

Figure 13 Concentration of urinary (aMT6s) and its correlation to fat oxidation
Pearson's correlation was used to understand the relationship between melatonin and fat oxidation.

Chapter 6: Tables

Table 1 Sleep architecture

	Dim	LED	OLED	p-value	η^2_G	*d* (LED vs. dim)	*d* (OLED vs. dim)	*d* (LED vs. OLED)
TIB	420	420	420					
TST	387.7 ± 9.7	396.6 ± 3.5	384.7 ± 8.2	0.481	0.046	0.38	0.11	0.60
Sleep latency	4.8 ± 1.7	5.7 ± 2.4	14.5 ± 8.4	0.281	0.076	0.13	0.51	0.45
SWS latency	21.6 ± 3.0	20.3 ± 4.3	30.4 ± 9.6	0.233	0.076	0.11	0.48	0.52
REM latency	120.8 ± 16.8	99.1 ± 14.2	109.7 ± 23.2	0.639	0.025	0.44	0.17	0.17
N1	45.9 ± 4.6	47.6 ± 6.8	44.8 ± 5.0	0.786	0.005	0.09	0.08	0.15
N2	199.6 ± 11.7	208.6 ± 13.1	194.7 ± 11.7	0.392	0.024	0.23	0.13	0.35
SWS	68.7 ± 9.0	66.6 ± 10.7	73.9 ± 7.9	0.496	0.012	0.07	0.19	0.25
REM	73.6 ± 9.2	73.9 ± 7.7	71.4 ± 6.8	0.870	0.002	0.01	0.08	0.11
WASO	27.9 ± 9.2	19.6 ± 2.2	21.2 ± 4.0	0.495	0.039	0.39	0.30	0.16

Overall sleep architecture shown with TIB, Time in bed; TST, total sleep time; SWS, slow-wave sleep; REM, rapid eye movement; N1, non-rapid eye movement sleep stage 1; N2, non-rapid eye movement sleep stage 2; WASO, wake after sleep onset; SE, sleep efficiency. Values expressed as mean ± SE, one-way repeated measures ANOVA, η^2_G indicates generalized eta squared, *d* indicates effect size between the light conditions defined by Cohen's *d*.

Table 2 Stage shifts

	Dim	LED	OEL	p-value	η^2_G	*d* (LED vs. dim)	*d* (OLED vs. dim)	*d* (LED vs. OLED)
N1 (n)	43.8 ± 4.0	45.3 ± 4.8	43.2 ± 3.6	0.812	0.005	0.11	0.05	0.16
N2 (n)	58.1 ± 3.7	55.4 ± 3.3	58.7 ± 3.8	0.675	0.017	0.24	0.05	0.30
SWS (n)	20.0 ± 3.1	19.9 ± 3.0	21.7 ± 2.8	0.621	0.009	0.01	0.18	0.20
WASO (n)	21.8 ± 2.1	23.2 ± 2.5	21.9 ± 2.1	0.771	0.009	0.19	0.01	0.18
REM (n)	9.9 ± 1.5	12.7 ± 1.4	11.6 ± 1.7	0.255	0.058	0.61	0.33	0.23
Total (n)	153.0 ± 9.6	156.0 ± 10.4	156.0 ± 9.0	0.925	0.003	0.09	0.12	0.02

Frequency of stage transitions indicated as mean ± SE. P-value of one-way repeated measures ANOVA. N1, non-rapid eye movement sleep stage 1; N2, non-rapid eye movement sleep stage 2; SWS, slow-wave sleep; WASO, wake after sleep onset; REM, rapid eye movement sleep. Values expressed as mean ± SE, one-way repeated measures ANOVA, η^2_G indicates generalized eta squared, *d* indicates effect size between the light conditions defined by Cohen's *d*.

Table 3 Oguri-Shirakawa Azumi MA version

	Dim	LED	OLED	*p*	η^2_G	*d* (LED vs. dim)	*d* (OLED vs. dim)	*d* (LED vs. OLED)
Sleepiness	47.0 ± 3.2	46.2 ± 3.2	47.0 ± 3.4	0.922	0.001	0.08	0	0.08
Initiation and maintenance of sleep	43.5 ± 1.5	41.9 ± 1.4	43.0 ± 1.9	0.712	0.02	0.37	0.10	0.22
Frequent dreaming	47.7 ± 4.6	47.2 ± 4.0	49.5 ± 4.4	0.916	0.007	0.03	0.15	0.19
Refreshing	48.8 ± 1.0	45.4 ± 2.7	44.8 ± 2.2	0.278	0.092	0.59	0.82	0.09
Sleep length	46.7 ± 2.7	43.0 ± 3.7	44.0 ± 3.8	0.537	0.028	0.40	0.29	0.09

Subjective sleep assessed from OSA is indicated as mean ± SE based on 5 categories. P-value indicate one-way repeated measures ANOVA, η^2_G indicates generalized eta squared, *d* indicates effect size between the light conditions defined by Cohen's *d*.

Table 4 Average values and effect size of energy metabolism

	Dim	LED	OLED	η^2_G	*d* (LED vs. dim)	*d* (OLED vs. dim)	*d* (LED vs. OLED)
Sleep							
EE	0.81 ± 0.01	0.80 ± 0.01	0.79 ± 0.01***	0.02	0.19	0.30	0.15
RQ	0.84 ± 0.004	0.85 ± 0.003	0.84 ± 0.003†	0.03	0.31	0.10	0.47
FOX	0.33 ± 0.02	0.28 ± 0.01**	0.32 ± 0.01††	0.06	0.53	0.09	0.60
COX	0.34 ± 0.01	0.35 ± 0.01	0.32 ± 0.01	0.01	0.06	0.18	0.26
Day 2							
EE	1.16 ± 0.02	1.13 ± 0.02*	1.10 ± 0.02**	0.03	0.21	0.43	0.21
RQ	0.889 ± 0.01	0.902 ± 0.01*	0.89 ± 0.01	0.03	0.37	0.04	0.32
FOX	0.33 ± 0.03	0.25 ± 0.02**	0.30 ± 0.02	0.05	0.53	0.18	0.40
COX	0.70 ± 0.03	0.71 ± 0.03	0.67 ± 0.03	0.01	0.11	0.15	0.25

Average (mean ± SE) of energy metabolism during sleep and on day 2. $^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$ significantly different from dim. $^{\dagger}p<0.05$, $^{\dagger\dagger}p<0.01$ significantly different between LED and OLED. Effect size indicated by generalized eta squared (η^2_G) and Cohen's *d*. EE, energy expenditure; RQ, respiratory quotient; FOX, fat oxidation; COX, carbohydrate oxidation.

Table 5 Average values and effect size of core body and skin temperature

	Dim	LED	OLED	η^2_G	*d* (LED vs. dim)	*d* (OLED vs. dim)	*d* (LED vs. OLED)
Sleep							
CBT	36.6 ± 0.04	36.6 ± 0.05	36.4 ± 0.05$^{***, \dagger\dagger\dagger}$	0.07	0.15	0.64	0.44
Distal temperature	34.6 ± 0.07	34.5 ± 0.07	34.4 ± 0.08	0.01	0.17	0.23	0.06
Proximal temperature	34.8 ± 0.06	34.6 ± 0.07**	34.9 ± 0.08††	0.1	0.34	0.10	0.38
DPG	-0.3 ± 0.08	-0.17 ± 0.07*	-0.42 ± 0.06†††	0.05	0.27	0.19	0.50
Day 2							
CBT	37.0 ± 0.04	36.9 ± 0.05	36.8 ± 0.05$^{***, \dagger}$	0.07	0.18	0.71	0.45
Distal temperature	32.2 ± 0.22	32.1 ± 0.23	32.1 ± 0.24	0.00013	0.08	0.04	0.03
Proximal temperature	34.1 ± 0.12	34.0 ± 0.08	34.3 ± 0.10	0.02	0.13	0.36	0.28
DPG	-1.9 ± 0.20	-1.9 ± 0.2	-1.7 ± 0.21	0.004	0.03	0.15	0.17

Average (mean ± SE) of core and skin temperatures during sleep and on day 2. $^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$ significantly different from dim light; $^{\dagger}p<0.05$, $^{\dagger\dagger}p<0.01$, $^{\dagger\dagger\dagger}p<0.001$, significantly different between LED and OLED. Effect size indicated by generalized eta squared (η^2_G) and Cohen's *d*. CBT, core body temperature; DPG, distal-proximal gradient.

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Material from: Ishihara, A., Metabolic responses to polychromatic LED and OLED light at night. Scientific Reports (2021).