Artificial Light at Night as a Health Risk Factor – Can the Effect of Different Illumination Sources be Measured?

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No doubt that Artificial Light at Night (ALAN) has brought economic prosperity to humans and prolonged nighttime socialization up to "24/7 non-stop cities". The increasing illumination world-wide results in increased electricity production on the one hand but also an increase in light pollution on the other. As far as the classical incandescent bulbs are concerned, most of their electrical energy is emitted as heat and thus CO2 production is expected to increase following the increased electrical demands for air conditioning particularly in closed spaces. The solution in regards to ALAN was moving to short wavelength (SWL) illumination, where Light Emitting Diodes (LEDs) are considered the ultimate "energy efficient" technology available today. However, the concerns we want to raise are related to the negative impacts of the LED technology on both the environment and human health. On June 2012 the American Medical Association (AMA) passed a resolution that ALAN is a source of pollution as among others, it suppresses production of the pineal hormone melatonin, which is typically produced under dark conditions. In order to assess the sensitivity of melatonin suppression under variant illumination sources we developed an animal model for estimating the association between melatonin suppression, epigenetic modifications and breast cancer development. Our results reveal significant differences between the tested illumination types.

Keywords: Artificial light - night - melatonin - epigenetic modifications - light pollution, illnesses

Biological background:

In ecological studies we distinguish between spatial and temporal variables. For many years the responses of organisms to spatial variables as a tool for assessing the changes in a given environment were relatively easy. For instance, our physiological understanding, of the thermoregulatory mechanisms in mammals, down to the molecular level made it easy to establish models for assessing physiological changes in response to changes in ambient temperature (Refinetti, 2010). However, our understanding of responses to temporal changes came much later only after establishing a relatively new biological discipline known today as chronobiology. The fact that terrestrial organisms have a "biological clock" (Ramkisoensing and Meijer, 2015) that controls distinctive endogenous rhythms (Circadian rhythms), entrained by the light/dark cycles known as a "time keeper" (Zeitgeber), is connected to the fact that these adaptive rhythms expected to be affected, if we interfere with the natural light/dark cycles with Artificial Light at Night - ALAN (Haim et al., 2005; Fonken and Nelson, 2014).

The mechanism of action by which light/dark cycles act as a "time keeper" became understood only after our better understanding of the structure and function of the photo-transduction pathway. Beyond the classical image-forming photoreceptors (IFPs) - cones and rods - the mammalian retinal bipolar

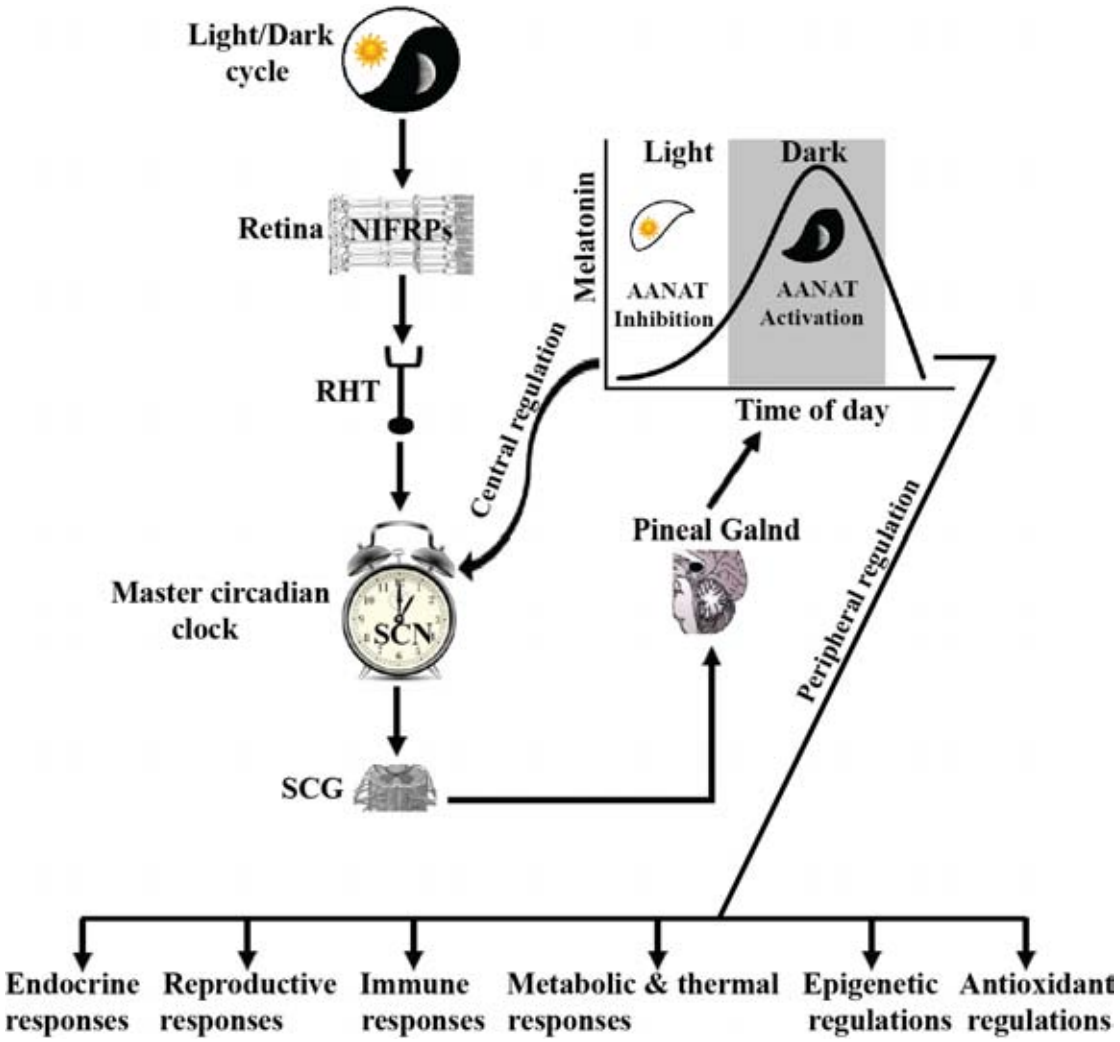


Figure 1: Regulation of the mammalian circadian system by light. The master circadian clock in the suprachiasmatic nucleus (SCN) is entrained by light via non-image forming retinal photoreceptors (NIFRPs) that project directly to the SCN throughout the retino-hypothalamic tract (RHT). The SCN conveys the circadian signal to the pineal gland via noradrenergic projections from the superior cervical ganglion (SCG). Arylalkylamine N-acetyl transferase (AANAT) plays a rate limiting step in the sequential synthesis of melatonin from serotonin; AANAT is activated during the dark phase and inhibited during the light phase. Melatonin rhythm is involved in regulating a variety of central and peripheral circadian related-processes. Fig adopted from Haim et al., 2013.

cells, express a distinctive class of non-image-forming photoreceptors (NIFPs) that contain the novel photo-pigment melanopsin (Berson et al., 2002). These bipolar cells distinguish only between light and dark signals and are intrinsically photosensitive even when the function of the IFPs is pharmacologically interrupted (Hattar et al., 2002; Bailes and Lucas, 2010; Pickard and Sollars, 2012). Furthermore, the melanopsin-containing NIFPs respond in a direct relation to light intensity and are highly sensitive to short wavelength (SWL) which are dominant at day time, with peak sensitivity at 480 nm (Brown and Robinson, 2004; Dacey et al., 2005; Berson et al., 2010). These characteristics make the NIFPs highly suitable for transferring the light/dark signals to the circadian system for controlling non-visual responses. The photo-transduction pathway by the NIFPs is elaborated in figure 1.

There are two important questions that emerge from the organization of the mammalian circadian system in regards to the retina structure and function:

1) Why did special photoreceptors as the NIFP evolved to mediate between the environment and the biological clock for controlling temporal organization?

2) How do they function within the mammalian circadian system? In placental mammalian

evolution, they had a long period of subterranean dwelling and in some species nocturnal activity when the Dinosaurs were the dominant animals above the ground during day time (Gerkema et al., 2013). Therefore, in the ancient mammalian environment, vision was not an important sense for survival. However, sensing the circadian information was crucial for survival in regards to daily activity and seasonal performance in reproduction, metabolism, and immune systems (Sharma, 2003). The "blind" mole rat *Spalax ehernbergi* is a recent subterranean mammal that shows this differentiation although considered blind it responds to changes in photoperiod, in regards to its thermoregulatory abilities (Haim et al., 1983). In regards to the function of the mammalian circadian system it is clear today that melanopsin is stimulated by SWL illumination and during the daytime (morning and afternoon) when they are dominant they suppress the melatonin production in the pineal gland.

Exposure to high intensity SWL illumination is a well-establish treatment for seasonal affective disorder (SAD) patients in high latitude countries that suffer from high melatonin levels in the plasma during daytime (Howland, 2009). Therefore, we must remember that SWL illumination is very efficient for suppressing pineal melatonin production at daytime. SWL illumination, resulting in low levels of melatonin during the light hours, is an important signal for the "biological clock", body cells, tissues and organs that it is daytime. With the disappearance of SWL from the environment in the late afternoon and the dark period the NIFP are not stimulated and the pineal gland starts producing melatonin from its precursor serotonin and thus the hormone accumulate in the pineal gland and thereafter release to the circulatory system during the dark hours (Cassone et al., 1993). However, SWL illumination even at level of 450 lux for a short period stimulates the NIFP resulting in the suppression of pineal melatonin (Cajochen et al., 2005). Among the existing lighting types known to date natural white and blue Light Emitting Diodes (LEDs) are highly efficient in blocking pineal melatonin production even in low intensities (Falchi et al., 2011; Haim and Portnov,2013).

Artificial Light at Night (ALAN):

One of the greatest inventions of the second half of the 19th century that changed human life in the most drastic way was the conversion of electrical energy into illumination. The development of the incandescent bulb by Thomas Alva Edison 1879 is a land mark in the long process where humans looked for ways to chase darkness away. No doubt that ALAN has brought economic prosperity, enabled us to socialize for many hours after sunset up to the creation of what we name today "Nonstop cities" - with activity of 24 h a day and seven days a week. If the illumination from the incandescent bulb covers a wide spectrum of the visible light it is considered an inefficient type of illumination as a great part of the electrical energy is converted into heat, emerging from the long wavelength illumination. Consequently, the CO_2 emission to the environment is expected to rise in response to increase electrical demands for air conditioning. Furthermore, the atmospheric CO_2 emission from burning fossil fuels in power plants is also expected to worsen as the electricity demands for illuminating public spaces (e.g., roads, streets, bill board, buildings, and shopping-centers, places of entertainment and private spaces) increase. Environmentalists were looking for ways to illuminate public and private space by efficient illumination where, most of the electric energy is converted into light and only an incremental amount is transformed into heat. So what is bad about saving energy and producing more light and releasing less CO_2 to the environment?

ALAN of SWL illumination increases light pollution and is a health risk factor:

In regards to increased light pollution, the move to highly efficient illumination is accompanied by a rebound effect. In the private space you increase illumination as the investment in the bulb is an act that takes place in a time magnitude of years while the reduction in the electricity bill is monthly so if you save money you can increase illumination, moreover, the intensity of the illumination sources increased. This will be applicable for countries that expenses on illumination are relatively high in comparison with other home electrical items as refrigerator, washing machine, dishwasher and others. In the public space intensities are increased no dimming of street and road lights, bill boards which are on all night. We must remember that increased public illumination affects our homes as light from outside may enter our sleeping habitats (Kloog et al., 2011). The American Medical Association (AMA) three years ago passed a resolution that light at night is a source of pollution among others because it suppresses melatonin production, disrupts daily rhythms and interferes with our sleep (AMA, 2012). From the literature we know that melatonin as a hormone is a "Jack of all traits" (fig. 1) therefore, we can assess that its suppression will result in a sever

health risk. What do we know about ALAN and health risk? Is the response to ALAN similar, for all spectral wavelength emission?

A Laboratory Model for Testing Effect of ALAN on Health Risk:

We established an experimental model for assessing the effects of ALAN on health risk using mice. Bearing in mind that to date we have no definition for ALAN as a source of pollution in regards to wavelength, intensity, duration of exposure, frequency and timing of exposure, we suggest that results obtained from our model can be used for establishing such a definition. Breast cancer, obesity and diabetes among others are increasing worldwide, is this increase related to the increase in light pollution? In our paper we will discuss the issue of breast cancer and light pollution as it is very well established due to the fact that these relations were first established in shift-workers (Haus and Smolensky, 2013) but today we are aware that it is a much wider phenomenon.

Our model is based on female BALB/c mice inoculated subcutaneously with 4T1 mice breast cancer cells. Due to this method, we can measure the tumor development with time under different environmental conditions, in our case different wavelengths illumination at the same intensity and with ALAN at the same exposure duration given at the same time during the dark period. In order to assess melatonin suppression we measure the content of the main melatonin metabolite 6-sulfatoximelatonin (6-SMT) in the urine. For this purpose we collect urine at different time-points during the 24 h cycle for constructing the daily rhythm production of the pineal hormone. After collecting the urine samples for over 24h, the mice are sacrificed, the tumor and other organs are removed and the organs in the body cavities are scanned for metastases. DNA is extracted from the tumor cells as well as other tissues for epigenetic studies where at the first stage assessing the modifications by measuring the levels of Global DNA methylation (GDM). Among three different types of illumination: incandescent, florescent and white LED the latter is the most risky to our health emerging from its wavelength, it has the highest ability for suppressing melatonin, thus we can show that low melatonin values coincide with both largest tumors and low GDM values. Such mice also have the highest rates of metastases. It is important to note that melatonin treatment to ALAN interfered mice attenuates the values, not only in mice exposed to LED but also in the other two groups (incandescent and florescent) which without the treatment show lower values of tumor volume, higher values of endogenous melatonin production and higher GDM values compared with those obtained for LED-exposed mice. Our results so far support the nexus between ALAN, melatonin suppression, hypo-GDM, and breast cancer development. Our results so far show that the wavelength of the illumination plays a major role and therefore, it should be considered by decision makers what type of illumination to use for ALAN. SWL-illumination which is typical for the day time natural illumination, cannot be used during the dark period. During the dark period the wavelengths that can be used are in the range of 560nm and above within the visual spectrum.

What should be the future of ALAN in regards to wave length?

As we are not planning to go back to the pre-Edison days, selecting the types of illumination should be an issue discussed by interdisciplinary groups in order to obtain a sustainable lighting. Like in any environmental issue the solution is not simple we cannot suggest the use of efficient illumination of a SWL when we know that it has a health risk as it suppresses melatonin production in an efficient way and disrupts daily rhythms. It may be a good solution on the short term but definitely not on the long term, national health expenses will increase dramatically and in regards to the social aspects it will be a burden on society emerging for instance from a dramatic increase in breast cancer incidences. One way to overcome this problem and still use the LED illumination is to eliminate the SWL peak by adding chemicals to the diodes but here, we need to be sure the features do not change with time in the case of public space where the LED light fittings will need to be checked on an annual basis in order to be sure they did not change their properties. The new Carbon bulbs are efficient as most of the electrical energy is converted into light with relatively minimal heat production. Maybe improving this type of illumination for instance by extending the life span of the bulb should be assessed. As this type of illumination has no SWL peak therefore, the suppression of melatonin production is minimal. We do suggest that further studies for improving intensity and other illumination properties should be carried out as defiantly it can become an indoor source of illumination.

It is time we should understand that ALAN is a source of pollution and its negative effects were not studied in a sufficient way. Therefore, national and international research funds should support interdisciplinary research in illumination in order to develop sustainable illumination which should be efficient and will enable us to work and enjoy our free

time after sunset. But, such an illumination should not have a negative effect on our environment and should not risk our health. If possible, it should not change the conditions in which the evolution of our temporal organization took place under darker nights (with no SWL illumination but with long wavelength illumination). If this will not happen and quite soon, apart of the human health risk we should expect serious reduction in biodiversity not only losing nocturnal species as these will not experience dark but it also may damage diurnal species which will increase activity into nighttime because of light pollution. At last but not at least, we should understand that lighting is an interdisciplinary topic and that all aspects should be studies in universities and technology institutes together with research in order to train professionals that will be able to find solutions to the many questions being raised.

Note:

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