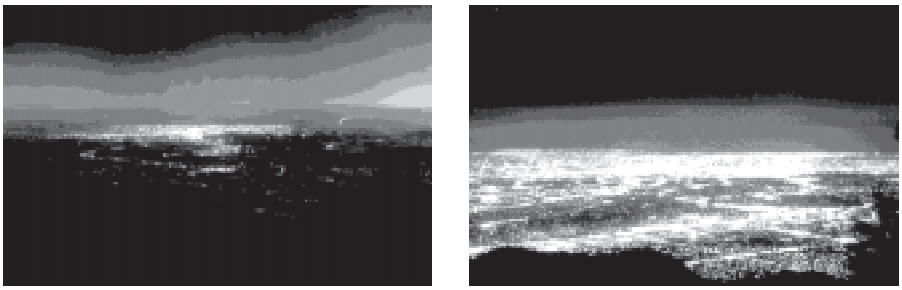
Meeting report

Light, endocrine systems and cancer

By Frank Gollnick

Evidence for the assumption that normal light – at the wrong place and at the wrong time – may pose a serious health risk for humans slowly, but steadily increases in importance as an object of scientific interest. The international symposium „Light, endocrine systems and cancer" having taken place on May 2 to 3, 2002, at the University of Cologne, particularly dealt with a potential increased cancer risk from nocturnal light („light at night") in the civilized world. In this context, obviously the association with the body hormone melatonin, produced by endocrine glands, plays a part also being of relevance for the discussion about health dangers from magnetic and electromagnetic fields. Interestingly, a new influential factor previously more or less ignored literally „sheds new light" on to-date scientific findings on disturbances in melatonin metabolism and the related cancer risk from field effects.



View of Los Angeles at night. To the left: 1908; right: 1988

Background

The „melatonin hypothesis" of R.G. Stevens (1987) well-known in science draws an association between external disturbances of melatonin release inside the body normally occuring during the night and a thus increased cancer risk, especially breast cancer. In our body, melatonin is seen as a hormonal „timer" regulating the normal day-night rhythm and thus also the normal sleep-wake rhythm. The pineal gland (an „endocrine" gland located in the human head) produces this hormone being controlled by light entering through the eyes. Between two and five o'clock in the morning, melatonin secretion normally is at its peak. Artificial light can dampen melatonin production or postpone the time of the main release. Also, melatonin is seen as a so-called scavenger of radicals in the whole body. A substance, that is, which can neutralize aggressive matters – the free radicals – attacking the genomic DNA in the body cells, thus in a certain way having cancer-inhibiting effects. In the past, a number of animal tests has provided evidence for a nocturnal decrease of the melatonin level caused by the influence of magnetic and electromagnetic fields. This way, the rate of experimentally induced breast tumors in rats increased. However, to date such evidence could not be repeated by multiple and/or independent replications. Thus, final proof is lacking.

The scope of the Cologne symposium

During the symposium taking place on May 2 and 3, 2002, at the Institute and Policlinic for Occupational and Social Medicine, and for Social Hygiene, University of Cologne, 13 lecturing scientists and a number of internationally renown experts presented evidence confirming the hypothesis that unnatural nocturnal light produced by artificial light sources could be a substantial reason for the steady increase in cancer cases. Both animal tests, mainly done in rodents, as well as population studies performed in certain limited groups

light

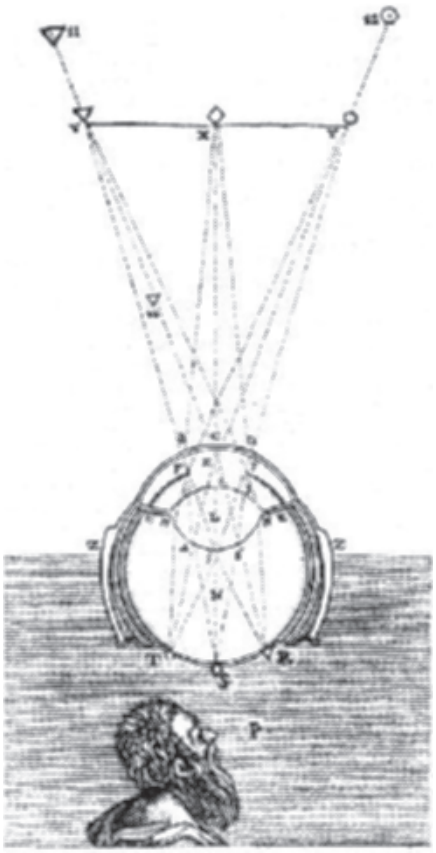
(blind people, night workers, people from nordic countries, etc), showed definite evidence for an association between a disrupted nocturnal dark phase and cancerous diseases. Added to this is the clear evidence that natural nocturnal melatonin production drastically suffers from artificial light perceived through the eyes. In the urban centers of our civilized and industrialized world, the use of nocturnal artifical light inside and outside houses has rapidly increased (see illustration on p. 59).

Experiments on animals and humans

Since the beginnings, oxygen and sunlight are two of the main regulators of physiological functions of living organisms existing on earth. The circadian (occuring in regular rhythms) organization of this functions for a long time solely was dependent on the course of the sun and related light-dark phases. Here, certain nerve structures in the ocular system and the pineal gland are key components maintaining the natural circadian rhythms in the body, as, for example, sleep phases. In this respect, melatonin that can reach all body cells via blood circulation, has a crucial messenger function. Melatonin signals nightfall to the body cells. Subsequently, during the nocturnal phase the body concentrates on its life-preserving regenerative functions. It is obvious that disruptions of this signal chain lead to malfunctions of the body and to diseases. Animal tests investigating certain artificially induced cancer types provided clear evidence that cancer risk increases if nocturnal melatonin production is reduced, fully suppressed or postponed by prolonged lighting of the cages, or even by short-term lighting and/or light flashes. Tests in humans examining effects on melatonin production point in the same direction. A new and amazing finding is how very small light intensities are sufficient to affect the production capacity of the pineal gland.

By coincidence, test animals provided first clues suggesting inexplicable variances of measured nocturnal melatonin levels across different test groups more or less unaccounted for by experimental measures or conditions. The reason for this was found only when scientists noticed that one of the test rooms where the animals were kept at night was invaded by pale, scarcely perceptible light through a small window in the corridor: even light with an intensity of 0.25 lux (!) at the site of the cages (scarcely perceptible by the human eye) leads to drastic setbacks of nocturnal melatonin increases in rodents. At night, and at this low light intensity, fatty acids and other blood parameters normally showing low levels in the dark, showed the same peaks as in tests using permanent lighting. If other tests on rodents instead artificially prolonged the night from normal 12 to 16 hours, growth of experimentally induced tumors was suppressed as effectively as by injection of additional melatonin portions. Similar results were reached in experiments done on isolated tumors in flow-through chambers as well as in cell cultures of human breast tumor cells (MCF-7 cells).

It was admitted that such tests also may show effects that have nothing to do with melatonin. Further comprehensive studies would have to include estrogen, prolactin, and other sexual hormones in order to exclude and/or consider interactions such as



Light and the human eye. In 1637, René Descartes discovered that light affects the pineal organ via the eye. Today we still try to understand the makings of these processes.

the sexual cycle or other circadian rhythms when interpreting results.

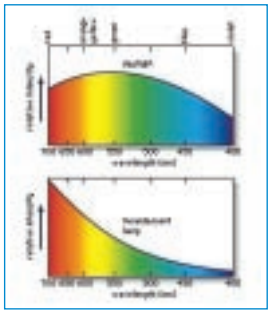
Experiments on test persons also showed that for affecting melatonin secretion it is not necessary, as previously assumed, to apply light intensities of 2,500 lux. Very carefully designed and performed experiments showed that even blue light with an intensity of 1.3 lux at the eye (100 lux for wide-band white light) may distinctly suppress melatonin production. These are light intensities far below normal room lighting or working light (300 to 500 lux). Nocturnal white light of 119 lux and below can clearly shift the daily human melatonin cycle. In this context, it was clearly concluded from above mentioned and other results that in the retina of our eyes, or in their vicinity, a hitherto unknown photo pigment would have to exist responding to a light wavelength of 464 nm (blue light) and being responsible for light stimuli conduction to the pineal gland. Definite evidence confirming this hypothesis is still lacking, though it is supported by several other findings presented in recent literature. A possible candidate for this new special function ocular pigment would be melanopsin which is found in ganglia cells (certain type of nerve cells).

Population studies

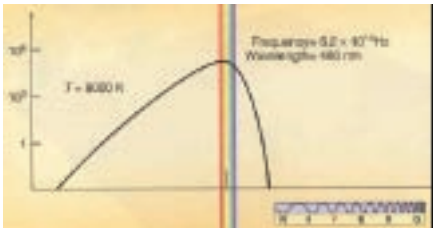
Obviously, also so-called epidemiological (population) studies provide evidence for an increased cancer risk from nocturnal exposure to artificial light, particularly for occupational exposure. However, in this part of the symposium it was unequivocally pointed out that it is quite difficult to accurately determine potential health risks such as of breast cancer for humans based on population studies. This is mainly because epidemiological studies require an adequate non-exposed control group for precise risk determination. Of course, regarding the problem of „light at night“, this is nearly impossible to do. In light of such predictable limitations, in Denmark and the United States recently three studies on night and shift workers were published independent from each other. With regard to the aim of achieving as precise test conditions as possible, these groups have the advantage of a *definitely* higher nocturnal light dose than control groups which do not work at night. The results of all three studies definitely pointed to an increased breast cancer risk in female long-term night and shift workers, even after the numbers were adjusted, that is, statistically corrected, by other known breast cancer risk factors. Other studies from the United States, Sweden, Finland and Norway on blind women, to a different extent (depending on the type of blindness) more or less shielded from light incidence at the retina, showed a by 20 to 40% decreased breast cancer risk compared to normal sighted control groups. Similar results were achieved when comparing Northern country populations (with long dark periods in the winter half year) with people living near the equator. Correspondingly, in populations living near the Arctic, an increased annual average of the melatonin level in the blood could be measured actually linked to a broadly decreased risk of hormone-related cancer types.

Repeatedly, in this context methodological limitiations of such studies were pointed to; these limitations were also lively and constructively discussed. Requirements for further epidemiological studies were listed, and new ideas for such studies were developed. For example, there should be more detailed information on actual nocturnal light exposure of individuals in statistical investigations. Deficiencies in (however difficult to perform) measurements of confounding factors should be dispelled, especially in the promising studies done in the above mentioned specific populations groups. So it was suggested to possibly extend tests to the group of „Amish people“ living rather secluded in the United States as some kind of „ideal control group“. They still try today to completely abstain from the use of electricity and other modern implements, therefore still being familiar with largely really dark nights.

The final lecture as well as the following final discussion emphasized the general willingness to do interdisciplinary research, as well as the – compared to the debate in other research fields – not very controversial discussion between experimental researchers on the one side, and epidemiologists on the other. Also, reservations concerning the partially very clearly appearing relations, hypotheses and interaction chains were uttered. The „new“ risk factor of „light at night“ related to circadian rhythms, for example, was seen critically insofar as industrialized countries not only did drastically change their handling of light, but as natural seasonal differences, in general, more and more lose importance. This is shown, for example, by our usual diet with its unnaturally regular input of certain nutrients throughout the year. The following questions were raised: How does the natural 25.5-hours rhythm embodied in ourselves (as found in experiments) and contradicting the externally determined 24-hours rhythm possibly affect cancerogenesis? How does our



Spectral composition of daylight (above) and artifical light (below)



Sun spectrum with visible light component

„genetic internal clock“ work? Is there a „clock gene“ determining our internal rhythm, or rather a metabolism process triggered by it?

As long as such questions remain unresolved, we would have to accept the fact that many „modern“ risk factors are „competing“ with each other and therefore should as far as possible be considered as disturbance factors when investigating the risk factor of „light at night“.

Conclusion

The symposium exemplarily showed that not only magnetic and electromagnetic fields are possible influential factors when dealing with melatonin homeostasis disturbances and, generally, with hormonally caused cancer diseases. Unnatural „light at night“ was definitely identified as a risk factor, even though there were certain methodological limitations. New common research efforts were established by setting more consistent goals.

One of the attending scientists quite personally summarized as follows: “As for me, I’ll pay a bit more attention to my personal ‘rhythm’ after listening to the scientists in Cologne; the alternative could be an increased cancer risk and I’m not very good at ‘singing the blues’.“

Abstracts of all meeting contributions, as well as four detailed rapporteur reports prepared by attending scientists with comprehensive references are found on the web at http://www.uni-koeln.de/symposium2002. Moreover, some results of recent studies on this topic are found at http://www.nel.edu/Press/Light-Endocrine-Cancer.htm.

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