There can be little doubt that man’s visual system provides him with critically important information about his environment. The individual who cannot perceive light and its reflections suffers an immense disadvantage; in the civilized world he is cut off from the written word, unable to use most tools, and poorly oriented; in the world of Nature his very survival is in constant jeopardy. The obvious significance of light in providing the substrate for vision has tended until recently to obscure the fact that light also exerts important biologic effects which are not dependent upon vision. Some of these effects of light are, like vision, initiated by responses of specialized photoreceptor cells in the retina. The photic input is transduced to nerve impulses which, instead of traveling to visual centers in the brain, terminate in brain regions that control glandular function. Other biologic effects of light result from direct effects of photic energy on the skin and the subcutaneous tissues. This report will summarize the former, neuroendocrine effects of light, and will comment on the latter. Recent experiments will be described which indicate that highly specialized pathways have evolved in the brain to mediate the extra-visual effects of light. The implications of these biologic consequences of light for the design of artificial light sources will be considered.

The Effects of Light on Glandular and Metabolic Functions

Environmental illumination acts as both an inducer and a timer of glandular and metabolic functions. Light (or its absence) induces or “turns on” the development of the gonads and the secretion of certain hormones. Thus, puberty develops earlier than normal in blind girls, and later than expected in the blind laboratory rat—a difference which may be related to the fact that humans are active diurnally, while rats are a nocturnal species. Darkness stimulates and light inhibits the production of hormones such as melatonin which are made in the pineal gland. Sudden exposure of human subjects to a bright light causes hydrocortisone to be released from the adrenal gland. Annual cyclic changes in the per cent of the 24-hour day represented by daylight, and the daily cycle of day and night serve as timers, or “time-givers.” These cycles synchronize a large number of biologic rhythms of similar periodicity which are probably generated by inborn “biologic clocks” in the brain. For example, all mammals appear to show daily rhythms in body temperature. This rhythm persists with a periodicity of about 24 hours in the absence of day-night cycles. However the times of day associated with maximum and minimum body temperatures can easily be shifted in the normal individual by varying the hours of the daily light period.

1. Inductive Effects of Light: Sexual Development

Four decades ago, W. Rowan, a Canadian biologist, first drew the attention of the scientific community to the ability of environmental lighting to induce or modify changes in gonad function in animals. It had been recognized that the gonads of most birds showed marked changes in weight as a function of time of the year; normally, the testes were largest during the spring and summer, and smallest during the winter. Rowan showed that the annual period of testicular growth in the junco finch could be made to occur prematurely, in the middle of the Canadian winter, by gradually increasing the number of hours each day that captive birds were exposed to artificial lighting. Control birds, which lived in “Riviera-like California,” did not develop sexually until springtime. Several years later, Bissonette showed that extra light could also induce a state of premature estrus in a mammal, the ferret, and Baker and Ranson demonstrated that this effect of light on the field mouse was not the result of...
changes in ambient temperature, humidity, or food intake.

The ability of light to modify gonad function had been recognized for some time: Dutch and Japanese farmers traditionally exposed song birds to extra illumination in the fall in order to induce singing—a behavioral consequence of testicular stimulation—in the winter. However, the demonstration that environmental lighting could specifically stimulate the gonads was of great importance in the history of endocrinology. It proved that the pituitary gland and the gonads were not related solely as a closed feedback system, but were also profoundly influenced by the external environment. It now became necessary for physiologists to characterize the biological machinery through which information about light was received by the body and translated into an endocrine message. It is now generally agreed that light activates photoreceptors which are connected to neural elements, and that special neuroendocrine organs must then transduce the resulting nervous stimuli into endocrine information. Four decades after Rowan, it seems clear that light is the most important environmental input, after food, in controlling bodily function.

In 1934, Hill and Parkes, and F. H. A. Marshall and Bowden showed that although extra light could hasten the onset of estrus in the ferret, light was not a prerequisite for normal sexual maturation, inasmuch as animals kept in constant darkness came into estrus (i.e., full ovarian function) at approximately the same time of year as those kept in natural lighting. Subsequently, it was shown that the gonads of blinded ferrets also became active at the normal time of the year, even though they could not respond to extra lighting with premature sexual maturation. Unlike the ferret, the white-crowned sparrow appears to have an absolute requirement for light in order to sustain seasonal gonad growth. Sexual development in the prairie dog appears to be entirely unaffected by environmental lighting. Exposure to continuous lighting profoundly alters ovarian function in the laboratory rat or mouse. In the hamster, the gonads show little response to constant light, but tend to atrophy when the animal is placed in continuous darkness. These observations indicate that there is wide variation among closely related species in the ways that gonad function responds to environmental lighting. Since adolescence comes so late in the human, and since the menstrual cycle takes so long (28-29 days), it has not been possible to do experimental studies on the effects of constant light or darkness or altered lighting cycles on human sexual function. However it has been shown that the absence of light perception has clear effects on the time of onset of puberty: We studied the age at which the first menstrual period occurred in about 300 blind girls, and an equal number of pair-matched girls with normal vision. Blindness due to disease of the eyes was associated with an earlier-than-normal menarche, such that the greater the loss of light perception in the patient, the earlier was the age at the first menstrual period. The rather small amount of data available on different species suggests that the absence of light induces gonad function in diurnally-active animals (e.g., humans, sheep) while the presence of light has this effect in nocturnal species (e.g., rat, ferret, raccoon, bat, cat).

2. Inductive Effects of Light: Synthesis of Pineal Hormones

The pineal gland of the mammal has undergone extraordinary changes with evolution. Among lower vertebrates (e.g., the frog), the pineal is not a gland but functions as a photoreceptor, or a “third eye.” It converts a photic input into nerve impulses, which are then transmitted to the brain. With evolution, the pineal has lost all trace of photoreceptive function; it no longer demonstrates a direct response to a light source, and no longer sends photic or any other information to the brain. Instead the pineal has developed into an unusual kind of gland—a neuroendocrine transducer. The mammalian pineal receives nervous messages from the brain, and responds to these by secreting a hormone, melatonin, into the bloodstream.

Even though the pineal of mammals is no longer directly receptive to light, its metabolic activity continues to be controlled by environmental illumination, but now indirectly: Photoreceptors in the eyes respond to environmental lighting by generating nerve impulses, which are transmitted along the optic nerve. Most of these impulses travel to brain centers which are associated with vision (e.g., the lateral geniculate bodies, the superior colliculi, the tegmental nuclei). However a small fraction of the impulses diverge from the main visual pathway and travel along a nerve bundle (the inferior accessory optic tract) which leads to the part of the brain that controls pituitary function (the hypothalamus), and, eventually, to the pineal gland (Fig. 1). Since the animal or human lives in an environment in which light and darkness alternate with 24-hour periodicity, the pineal receives a large number of nerve impulses for about 12 hours each day, and a small input for the alternating 12-hour period. The pineal responds to these nerve impulses by making more or less of its hormone, and also by changing in weight and histologic appearance. When rats are placed under continuous darkness, their pineal glands enlarge and secrete large amounts of melatonin. When the animals are placed under continuous light, the pines shrink, and make very little melatonin. The melatonin enters the circulation, and is delivered to organs.
The precise locus at which light information appears to control melatonin synthesis is at the production of an enzyme, hydroxyindole-O-methyl transferase. This enzyme, which is stimulated by darkness, is required to catalyze the last step in melatonin biosynthesis. Darkness also causes more noradrenaline to be released from nerve endings in the pineal; this compound probably acts to induce the enzyme. Light has the opposite effect. If animals are blinded or are placed in continuous light or darkness, the 24-hour rhythm in the activity of the melatonin-forming enzyme is immediately lost. The same effect is observed if the nerves to the pineal gland are cut, or if the brain pathways which mediate the endocrine effects of light (i.e. the inferior accessory optic tract, described above) are damaged.

3. Synchronization of Daily Endocrine Rhythms by Day-Night Light Cycles

The first evidence indicating that glandular or metabolic function in humans varied according to time of day was obtained by Gregory Pincus, in 1943. It had been shown that some of the steroid hormones secreted by the adrenal gland appeared in the urine as a characteristic group of metabolites, the ketosteroids. Pincus showed that the urinary ketosteroid levels of healthy young men were significantly lower in samples collected at night than in those excreted during the daytime. He suggested that this difference reflected 24-hour periodicity at which the steroid hormones, especially cortisol, were secreted from the adrenal gland. This hypothesis was subsequently confirmed when sensitive chemical techniques were developed for measuring the levels of adrenocortical hormones in blood. The presence of a day-night rhythm in adrenocortical secretion now constitutes a standard, highly sensitive test of adrenal function which is available in most major hospitals.

A large body of information has been accumulated concerning diurnal rhythms in endocrine gland activity and in consequent metabolic events. Most of these rhythms can be modified experimentally by varying lighting schedules. For example, the concentration of one kind of white blood cell, the eosinophile, in the blood of the mouse fluctuates with a diurnal cycle. Animals kept in light during the day and in darkness at night show peak blood eosinophile concentrations at noon, just before the rate of adrenal secretion starts to increase. If the start of the daily light period is moved forward by 12 hours, the time of the peak in blood eosinophile concentration is shifted by an equal number of hours after nine days of exposure to the new lighting conditions. If mice are placed in constant darkness, the eosinophile cycle persists at about 24 hours in length. When the animals are exposed to continuous lighting for nine days, the eosinophile cycle disappears; how-
ever it can be renewed if the mice are returned to cyclic illumination.\textsuperscript{29} These data suggest several characteristics of the diurnal blood eosinophile rhythm of mice (and the underlying adrenal secretory rhythm): (1) it does not have an absolute requirement for cyclic light changes, and hence may represent an "endogenous" rhythm; (2) however, it is normally synchronized by the day-night light cycle; and (3) it is subject to marked perturbation, even extinction, in the presence of abnormal lighting conditions.

Many endocrine functions in birds and mammals have now been shown to demonstrate 24-hour periodicity. These include: (1) the secretion of corticosteroids from the adrenal in mice,\textsuperscript{29} rats,\textsuperscript{30} monkeys,\textsuperscript{31} and humans;\textsuperscript{32} (2) the level of ascorbic acid in the ovary of the pseudopregnant rat,\textsuperscript{33} the release of the hormone which causes ovulation in chickens,\textsuperscript{34} and the time of day that the guinea pig ovulates;\textsuperscript{35} (3) the content of the hormone which causes lactation in the pituitary gland of the rat;\textsuperscript{36} (4) the level of calcium in the serum of humans suffering from hyperparathyroidism;\textsuperscript{37} (5) the activity of renin, a substance which elevates blood pressure, in the plasma of normal humans;\textsuperscript{38} (6) the level of the thyroid-stimulating hormone in the blood\textsuperscript{39} and pituitary\textsuperscript{40} of the rat, and the secretion of thyroxine from the cat thyroid.\textsuperscript{41}

A large number of metabolic events which depend upon the adrenal gland also show 24-hour periodicity, in response to the 24-hour rhythm in adrenocortical secretion. These include rhythms in the amounts of glycogen, RNA, DNA, and phospholipids in the livers of rats, the number of dividing cells in the liver and the adrenal cortex, susceptibility of the animal to the toxic effects of certain drugs, and a growing list of related functions.\textsuperscript{4} In addition, very important and obvious rhythms exist in human and animal behavior (i.e., sleep-wakefulness, activity, time of eating) and in body temperature; the mechanism of these rhythms are probably independent of the endocrine rhythms.

In the past few years, studies have been initiated on the mechanisms responsible for 24-hour rhythms in bodily function. By use of experimental models in which animals are deprived of various cyclic inputs from the environment (e.g., dark-light; food ingestion; environmental temperature and humidity rhythms), it has been possible to separate rhythms into three groups.\textsuperscript{42}

\textbf{A. Exogenous Rhythms:}

These rhythms are generated by an input of cyclic information from the environment. Thus far, only the daily light cycle and feeding rhythm have been shown to be able to generate biologic rhythms. The normal mammal shows marked daily rhythms in the activity of the pineal enzyme (described above) which makes the hormone melatonin,\textsuperscript{23} and in the activity of a liver enzyme, tyrosine transaminase, which regulates the metabolism of dietary proteins.\textsuperscript{23} The pineal rhythm is generated by the light-dark cycle: It is immediately extinguished when animals are blinded or are placed under continuous darkness.\textsuperscript{23} (The 24-hour rhythm in the concentration of noradrenaline in the pineal shows a similar response to the loss of the light-dark cycle). The liver rhythm represents a response of this organ to the cyclic ingestion of dietary protein.\textsuperscript{44} The normal rat (or human) eats for several hours of the day, then undergoes a prolonged fast for eight to twelve hours. (The period of fasting coincides with part of the daylight hours for the rat, and with nighttime for the human.) Hence the liver is exposed to large amounts of dietary protein for part of the day, and to no dietary protein for the rest of the day. In response to dietary protein, the liver makes more of the tyrosine transaminase enzyme. This enzyme rhythm can be extinguished if the experimental animal is deprived of dietary protein, or if it is made to eat small meals throughout the 24-hour day. If the animal is suddenly placed in an environment in which the lights are on from 6:00 pm to 6:00 am instead of 6:00 am to 6:00 pm, its eating cycle will gradually accommodate to the new lighting rhythm, and the phasing of the enzyme rhythm will change simultaneously.

\textbf{B. Circadian Rhythms:}

These rhythms appear to persist even when all cyclic environmental cues are removed from the animal. Moreover, their periodicity changes from exactly 24 hours to something more or less; for example, they may "free-run" at 23 hours and 15 minutes.\textsuperscript{43, 45} This suggests that the oscillator responsible for the rhythm resides within the animal, that it does not generate perfect 24-hour cycles, and that its signals are normally locked at exactly 24 hours by cyclic cues from the environment. Such rhythms include those of body temperature, eating, adrenocortical secretion, and the activity and sleep cycles; in all cases, environmental lighting provides the dominant "time-giver" for the endogenous oscillator.

\textbf{C. Endogenous Rhythms:}

These rhythms, which constitute the bulk of the known 24-hour rhythms,\textsuperscript{1} persist when specific environmental cycles are abolished; hence it is possible that they are generated by an endogenous source. However, it has not yet been shown that they "free-run" in a constant environment. Hence it is also possible that they are exogenous, and that they represent responses to untested environmental cycles (e.g., in magnetic field strength or cosmic rays) and
are not the result of endogenous oscillators. Unfortunately, economic considerations tend to keep most rhythms in this scientific limbo. The study of most rhythms involves killing the experimental animal to obtain the rhythmic tissue. Hence it becomes prohibitively expensive to try to demonstrate, for example, a change in cycle length from 24 hours to 23 hours and 45 minutes in the liver RNA content of the blinded rat.

Environmental lighting is thus seen to interact with all 24-hour rhythms; it generates or induces certain exogenous rhythms, and synchronizes circadian and other endogenous rhythms. The temporary impairment of well-being and intellectual function associated with West-East travel is certainly well known to this community. It doubtless results in part from the desynchronization in 24-hour rhythms caused by the differing number of days that individual rhythms need to accommodate to the new lighting schedule. We have very little information on the possible ill effects of the absence of a 24-hour light-dark cycle on space travellers. However, it would seem obvious that additional research on this problem should be a prerequisite to the planning of extended space missions.

4. Physical Characteristics of Light Sources Which Modify Endocrine Function

Just as lighting engineers have tended to overlook the biologic effects of light that are not related to vision, biologists have tended to overlook the fact that light is not a homogenous entity which exists in two states ("off" and "on"). Although there is an enormous literature on the inductive and synchronizing effects of light in mammals, one can count on a single hand all of the papers which have attempted to examine which portions of the photic spectrum are biologically effective, and what order of light intensity is needed. Few if any data are available about the action spectra for the effects of light on the mammalian gonads or pineal, or for the kinds of light which can entrain rhythms. It is not even possible to hazard a reasonable guess as to whether the retinal photoreceptor which initiates these responses is a rod cell, a cone cell, or something else.

Some measurements have been made on the photo-endocrine action spectra of lower vertebrates. However, these data are of questionable relevance to man, inasmuch as the responses in lower vertebrates appear to involve extraretinal photoreceptive organs which probably do not exist in man. For example, Benoit has shown that long-wavelength visible lighting is most effective in stimulating testicular growth in drakes; however this light produces its effect by acting on a brain photoreceptor (in the hypothalamus) which is absent in mammals. A single study by Marshall and Bowden showed that long-wave-length ultraviolet light (3650 Å) was most effective in stimulating gonad growth in the secrect. We are presently attempting to extend these findings.

Data on the threshold level for endocrine responses to light are also fragmentary. Farner has shown that ferrets have an "all or none" response to extra lighting, once a level of 9.3 fc is reached. Browman demonstrated that time of lighting was more critical than level by showing that rat ovaries were not abnormally stimulated by direct summer sunlight presented in the daytime, but could respond to a 30-footcandle artificial light source presented continuously. Bartholomew studied the relation between light level and testicular growth in sparrows exposed to light for 16 hours per day. When the level was increased from 0.04 to 10.3 footcandles, there was an increase in the rate of gonad growth; however, levels of 50 to 250 footcandles were no more effective than 10 footcandles. Wilson et al. found that it was possible to make light level the limiting factor in the rate of sexual development in Leghorn chickens by restricting the hours and frequency of light exposure. Under these conditions, animals reared in 0.04 footcandle matured less rapidly than those kept in 0.4 to 6.6 footcandles of light; chickens exposed to 0.5 to 30.0 footcandles matured most rapidly. As little as one footcandle of light is adequate for optimal egg production by chickens, and for stimulating the testes of drakes. Although relatively little information is available relating the level of light exposure to its efficacy as a neuroendocrine stimulus, it seems likely that the range in which the level may be rate-limiting in mammals is well below that provided by the systems of artificial illumination generally in use.

Biologic Considerations in the Development of Artificial Light Sources

From the information currently available, what conclusions can the lighting engineer draw about the biologic effects of lighting which might help him in the design of light sources? One fact seems certain: Light has biologic effects, and they may be very important to the health of the individual. Data have been available for some time showing that environmental lighting influences "well-being," performance, and other biologic phenomena which are difficult to measure. Recently evidence has begun to accumulate that light exerts specific biologic effects, which are easily measured and reproduced in the experimental laboratory. These effects are of two kinds: (1) Those which modify the individual's endocrine and metabolic state, and which are mediated through the retinas; and (2) Those which result from a direct action of light on the skin (e.g. stimulation of Vitamin D production, skin tanning, photolytic dissociation of bilirubin). While the action...
spectrum for the latter effects are still not well known, the general spectral regions involved are, and these are absent from the spectra provided by most commercial light sources. The action spectra for the inductive and timing effects of light on glandular and metabolic function are barely known at all. However, their definition will almost certainly be possible within the next few years, and may prove to be important to the illumination engineering community. In the interim, what kind of light sources should we construct in order to satisfy man’s biologic as well as visual needs?

Over the eons past, natural light has, of course, been the dominant illumination under which the physiologic action spectra have arisen. The duplication of this light within the range of its variations would therefore seem to be a logical goal of illuminating engineers until further research dictates an improvement.

References


DISCUSSION

John Ott:* Dr. Wurtman's paper presents data demonstrating direct responses of endocrine functions in the pineal gland to light stimulus entering the eye. It is of tremendous significance in that it suggests an explanation of the mechanism responsible for many photobiological reactions. This data goes far in providing the vitally important missing link of information between the work of a number of scientists who have observed certain photobiological responses in different species of animals, including humans, and others who have observed and drawn detailed diagrams of direct connections between the retina and the hypothalamic region of the brain, including in particular both the pituitary and pineal glands.

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As Dr. Wurtman suggests, the significance of these connections which are independent of the optic nerve may not have been fully recognized in the past because of the primary importance of the function of vision. Better interdisciplinary communications are needed between the fundamental research scientist, the illuminating engineer and the physician, in order to correlate not only existing knowledge, but especially new findings in the field of photobiology, photophysics and photoendocrinology. As Dr. Wurtman has pointed out, it is now clear that light is the most important input, after food, in controlling bodily functions.

Although most of the published data at present on photo-biological responses deal primarily with circadian rhythms and gonadal development, additional biological responses have been noted in laboratory animals kept under different light spectra. Reports in Today’s Health, published by the American Medical Association, the Illuminating Engineering Society’s journal and other publications, suggest that the action spectra of light may influence the determination of sex, tumor development and various physiological and psychological functions.

The formation of the Joint AIA-AMA Committee on Environmental Health, and studies combining the disciplines of endocrinology and the physics of light energy by the Massachusetts Institute of Technology are outstanding examples of progress toward the improvement of interdisciplinary communications. The interest shown by members of the Illuminating Engineering Society in the presentation of papers such as Dr. Wurtman’s on “The Biological Implications of Artificial Illumination” should go far in encouraging much needed additional work at this still embryonic stage of development of research into light and its effects on human environment.

The most significant implications of Dr. Wurtman’s paper to the immediate interests and concern of the illuminating engineer would seem to be his stressing that biological reactions over the past centuries have arisen under the action spectrum of natural light, and that duplication of this light within the range of its variations would therefore seem to be a logical goal until further research dictates an improvement.


*Author.

Richard J. Wurtman: I would like to thank Drs. Ott and Logan for their gracious comments.

HENRY L. LOGAN: The importance of this subject to lighting engineers is highlighted by this paper from one of the most highly respected and soundest authorities in the biomedical field. It is a significant coincidence that the two-inch-thick tome, “Spectrum Engineering—The Key to Progress,” authored by the Joint Technical Advisory Committee of the IEEE and the EIA, has just appeared in print. The next great step forward in artificial lighting is through the gateway of “Spectrum Engineering.”

Dr. Wurtman points out, with a wealth of scientific evidence to back up his conclusion, that “artificial light sources should be modified to become compatible with biologic needs,” and lighting engineers should be encouraged to use “natural light (or spectral facsimiles) in modern artificial environments.” The urbanization of modern man, which gathers him into megalopolitans of such huge size that it is impossible for daylight to penetrate more than fifteen feet into the perimeter areas, makes reliance on “spectral facsimiles” a must, in the great majority of structures in which people learn and work. I would like to call particular attention to an apt phrase of Dr. Wurtman’s, namely, “the extravisual effects of light” and his conclusion that “light is the most important environmental input, after food, in controlling bodily function.” I have been saying this in various ways, on the basis of natural environmental evidence, for thirty years, and I can only welcome the irrefutable data which Dr. Wurtman has presented. I hope that lighting engineers will agree with Dr. Wurtman that the “duplication of this light within the range of its variations is a logical goal” for lighting engineers. The idea that artificial light is an expense, to be cut as much as possible, still lingers. That is why the lighting industry has spent so much effort on what was nearest its nose—finding out what is the minimum lighting level at which a particular usual operation can be acceptably performed, instead of finding out how much and what kind of light is needed to promote health, reduce the rate of aging, and increase both the useful life of people and their total life.

These more fundamental and larger objectives appear to require higher levels of light than are needed for conscious seeing, and only now are we arriving at a standard of living which permits us to consider what is involved in this larger view. Dr. Wurtman’s paper is a welcome step along this road.

Gold Medal Nominations Due January 1

The Managing Director invites all IES members to submit nominations for the 1969 Gold Medal. The award is for “meritorious achievement which has conspicuously furthered the profession, art or knowledge of illuminating engineering.” Nominations must be received at IES Headquarters, 345 East 47th St., New York, N.Y. 10017, by January 1. Nominees need not be members of the Society nor citizens of the United States.

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