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This study assessed the effects of bright light on biological and behavioral measures to determine if bright light can reduce fatigue and enhance human work performance. Female subjects (N=37) were exposed to one of 3 lighting conditions in a between groups research design. Subjects in the bright light groups were exposed to 5000 lux white light from 1800 hrs to 2400 hrs (Early Bright) or from 2400-0600 hrs (Late Bright from 1800-0600 hrs (Dim Red). Blood sample were taken every 90 minutes. Repeated measures ANOVA indicated a significant interaction effect (light x time) for tympanic temperature, (F=3.339, p=.001). The bright light conditions maintained highter tympanic temperatures from 2300 hrs through 0400 hrs. Plasma melatonin measures indicated a main effects difference of F=4.009, p=.029. Most importantly, the results showed that the "light" x "time of night" interaction for melatonin was significant at F=59.436, p=.000. The suppression of plasma melatonin was greatest from 2230 hrs through 0500 hrs in the Early Bright and Late Bright groups. Cortisol was not affected by the ambient lighting conditions. Dim red light resulted in higher scores

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and Dim Illumination upon Circadian Neuroendocrine, Electrophysiological and Behavioral Measures.

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1992 FINAL TECHNICAL REPORT

EFFECTS OF EARLY BRIGHT, LATE BRIGHT AND DIM ILLUMINATION UPON CIRCADIAN
NEUROENDOCRINE, ELECTROPHYSIOLOGICAL, AND BEHAVIORAL RESPONSES

Submitted for Consideration By

AIR FORCE OFFICE OF SCIENTIFIC RESEARCH

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ABSTRACT

BRIGHT LIGHT SUPPRESSES MELATONIN AND IMPROVES COGNITIVE PERFORMANCE DURING NIGHTTIME HOURS IN HUMANS P Hannon*, G Brainard, R Childs, W Gibson, J French, J Hanifin and M Rollag. Northern Arizona University, Coll. of Health Prof., Flagstaff, AZ.,86011; Armstrong Laboratory/CFTO-Brooks AFB, Jefferson Medical College, and Uniformed Services University-Health Sciences.

This study assessed the effects of bright light on biological and behavioral measures to determine if bright light can reduce fatigue and enhance human work performance. Female subjects (N=37) were exposed to one of 3 lighting conditions in a between groups research design. Subjects in the bright light groups were exposed to 5000 lux white light from 1800 hrs to 2400 hrs (Early Bright) or from 2400-0600 hrs (Late Bright). The third group of subjects received 50 lux of red light from 1800-0600 hrs (Dim Red). Blood samples were taken every 90 minutes. Repeated measures ANOVA indicated a significant interaction effect (light x time) for tympanic temperature, (F=3.339, p=.001). The bright light conditions maintained higher tympanic temperatures from 2300 hrs through 0400 hrs. Plasma melatonin measures indicated a main effects difference of F=4.009, p=.029. Most importantly, the results showed that the "light" x "time of night" interaction for melatonin was significant at F=59.436, p=.000. The suppression of plasma melatonin was greatest from 2230 hrs through 0500 hrs in the Early Bright and Late Bright groups. Cortisol was not affected by the ambient lighting conditions. Dim red light resulted in higher scores on the Stanford Sleep Scale from 2400 hrs through 0500 hrs (light x time, F= 2.595, p=.023). Subjects under the bright light conditions performed better on the cognitive measures of Code Substitution accuracy (F= 3.918, p=.030) and Column Addition accuracy (F=4.660,p=.017). These data show some improvements in cognitive performance and alertness associated with bright light exposure and occur with changes in tympanic temperature and plasma melatonin at critical time periods.

EFFECTS OF EARLY BRIGHT, LATE BRIGHT AND DIM ILLUMINATION CIRCADIAN
NEUROENDOCRINE, ELECTROPHYSIOLOGICAL, AND BEHAVIORAL RESPONSES

Significance, Aims and Objectives

Currently, illumination levels are specified for military use for different tasks and environments ranging from about 50 lux for computer monitor display work to approximately 3500 lux for such tasks as reading # 4 pencil handwriting and machine repair (Mil-Std-1472C, 1981, pp 167-169). However, specified illumination levels are usually selected for optimum vision for specific tasks without factoring in potential biological effects of lighting on people which only become apparent after relatively long duration performance on work tasks. Human performance may be less than optimal under the 5 to 50 lux light environment that is typical of many control room settings. Further, in military or civilian control room settings, a decrease in attention or a decrement in cognitive processing due to less than optimal levels of lighting could pose a serious safety problem. Night shift personnel and task managers (eg. military officers and skilled military labor) who manage their sleep schedule improperly may be especially sensitive to this lighting variable. Military settings such as Air Transport and Air Weapons Control Systems demand that their people be at an optimal level of cognitive performance throughout their work shift. Moreover, there are implications for the transportation industry and for nuclear power plant operation. The Three Mile Island and Chernobyl nuclear accidents, and the Bhopal chemical disaster are three of the many examples of human error mediated accidents occurring during the early morning hours (Mitler et al., 1988). It would seem that tasks that are monotonous and yet demand peak vigilance would be most sensitive to performance fluctuations during the circadian cycle (Monk, 1987).

In addition to the cognitive and affective measurements, simple closed motor task measurements (grip strength-dominant hand) were also measured in the present protocol. Physical effort is known to be affected by desynchronisis or jet lag (Wright et al., 1983). Therefore, grip strength allowed the examination of the effect of bright illumination on muscular strength during a sustained nighttime performance. This is new ground in the exercise science discipline (Sage, 1984).

Report of Status of the Current Research Effort

Data collection on 37 women was completed in December, 1991. This collection was accomplished on 19 weekend sustained operation experiments. Data reduction to date includes results on the tympanic temperature, cortisol, melatonin, and behavioral measures. A decision was made on the present research effort not to collect electrophysiologic data due to the technical problems in collecting the data and

the problems involved in the meaningful statistical analysis of EEG data.

Dr. Jon French at Brooks AFB will be reducing the Actigraph data in the near future. A paper will be ready for submission to Brain and Behavior by November, 1992.

Please see the abstract for a more detailed list of results.

Other accomplishments in the form of abstracts, presentations, and papers related to the present research effort are listed below:
List of scholarly works:

Patrick Hannon- First Author-relevant to the present research effort

Oral Presentation
Hannon, Patrick, "Illumination and human performance" - presented July 27, 1989, Brooks AFB Summer Seminar Series.

Abstract-
Hannon, Patrick, Brainard, Gibson, William, French, Jon, Arnall, David, Brugh, Lisa, Littleman-Crank, Cynthia, Fleming, Scott, and Howell, Brian "Effects of bright illumination on oral temperature and cognitive performance in humans during nighttime hours" Association of Professional Sleep Societies, June, 1991 meetings.

Abstract
Hannon, P.R., G.C. Brainard, W. Gibson, J. French D. Arnall, L. Brugh, C. Littleman, S. Fleming and B. Howell, Effects of bright wide spectrum illumination on sublingual temperature and cognitive performance in humans during nighttime hours. Sleep Res 20:458, 1991.

Abstract
Hannon, P.R., G.C.Brainard, W. Gibson, J. French, D. Arnall, L. Brugh, C. Littleman-Crank, S. Fleming, J. Hanifin and B. Howell. Effects of bright illumination of sublingual temperature, cortisol and cognitive performance in humans during the nighttime hours. Photochemistry and Photobiology 53:15S, 1991.

Abstract
Hannon, Patrick, Brainard, Gibson, William, French, Jon, Arnall, David, Brugh, Lisa, Littleman-Crank, Cynthia, Fleming, Scott, Hanifin, John, Howell, Brian and Mark Rollag (1992) Bright light suppresses melatonin and improves cognitive performance during nighttime hours in humans. Association of Professional Sleep Societies, June, 1992 meetings.

Published Papers- George Brainard- relevant to the present research effort

French, J.,J. Whitmore, P. Hannon, G.C. Brainard, and S. Schiflett Photic effects on sustained performance. In: Space Operations and Research (SOAR), a NASA publication (in press).

Brainard, G.C. Biological Effects of Light in Humans: The regulation of physiology, mood and behavior. In: Biologic Effects of Light (Holick & Kligman, Eds.) New York: Walter de Gruyter & Co. (in press)

Gaddy, J.R., M. Edelson, K. Stewart, G.C. Brainard, and M.D. Rollag, Possible retinal spatial summation in melatonin suppression. In: Biological Effects of Light (Holick & Kligman, Eds.) New York: Walter de Gruyter & Co., (in press)

Sanford, B., G.C. Brainard, S. Beacham, J. Hanifin, J. Markoff, L. Streletz, P. Hannon, and D. Sliney Dose-dependent effects of UV-A on visual evoked potentials in humans. In: Biological Effects of Light (Holick & Kligman, Eds.) New York: Walter de Gruyter & Co., (in press)

Published Abstracts- George Brainard- relevant to the present research effort

Schiffman J.S., M. Glover, S. Miller, M.D. Rollag, and G.C. Brainard Pineal melatonin suppression in rats with electroluminescent light: potential application for use in space. American Assoc. Advancement of Science, Annual Meeting, Washington, D.C. February 17, 1991.

Barker, F.M., G.C. Brainard and P. Dayhaw-Barker. Transmittance of the human lens as a function of age. Invest. Ophthalmol. Vis. Sci. Suppl.32:1083.

Edelson, M.I., S.P.Tirney, J.R. Gaddy, K.T. Stewart, and G.C. Brainard Effect of light intensity on oral, rectal and tympanic temperature and full body activity. Sleep Res. 20:454, 1991.

Gaddy J.R., M.I. Edelson, K.T. Stewart, M.D. Rollag and G.C. Brainard Differential melatonin suppression despite equal corneal illuminance. Society for Light Treatment and Biological Rhythms, Toronto, Ontario, June 13-14, 1991.

Brainard, G.C., J. French, P.R. Hannon, M.D. Rollag, J.P. Hannon and W. Storm, The influence of bright illumination on plasma melatonin, prolactin, and cortisol rhythms in normal subjects during 30 hours of sustained wakefulness. Sleep Res. 20:444, 1991.

Brainard, G.C., S. Beacham, J.P. Hanifin, D. Sliney and L. Streletz, Regulation of circadian and neuroendocrine physiology by ultraviolet radiation. Second Internat. Conf. Biological Effects of UV-A Radiation, San Antonio, Texas, June 26-28, 1991.

Copies of selected abstracts, papers listed above are included with this Final Technical Report

BRIGHT LIGHT SUPPRESSES MELATONIN
AND IMPROVES COGNITIVE PERFORMANCE DURING NIGHTTIME HOURS IN HUMANS

Patrick Hannon, George Brainard, William Gibson, Jonathan French, David Arnall, Lisa Brugh, Cynthia Littleman Crank, Scott Fleming, John Hanifin and Mark Rollag

Northern Arizona University, USAF Sch. Aerospace Med., Brooks AFB, Jefferson Medical College, and Uniformed Services University-Health Sciences

The objective of this study was to assess the effects of bright light on plasma cortisol, melatonin, glucose, lactate and behavioral measures to determine if bright light can affect these correlates, reduce fatigue and enhance human work performance during specific nighttime periods. **Methods:** Twelve senior Air Force ROTC male cadets, ages 21-29, were exposed to 2 lighting conditions in a counter-balanced design to evaluate a) order of presentation effects b) time of night effects and c) illumination condition (bright v. dim) effects across the 7 respective measurement periods from 2130 hrs through 0800 hrs. On one night, subjects were exposed to 5000 lux white light (Vita-lite, Duro-test Corp.) from 2100 hrs to 0800 hrs. During the other night, subjects were exposed to dim illumination (50 lux) throughout the night. Blood samples were taken every 90 minutes, centrifuged and stored at -80 C until assay. A minimum of two weeks separated these 2 nights of experimentation. Cortisol and melatonin were assayed by RIA. Glucose and lactate were assayed using enzymatic techniques. **Results:** As reported previously, a repeated measures ANOVA showed that subjects had significantly ($p<0.001$) higher oral temperature and significantly ($p< .02$) improved cognitive performance from 2100 hrs to 0800 hrs when exposed to bright v. dim illumination (Hannon et al.,1991). Subjects had typical nocturnal rhythms of plasma cortisol with no significant effects of bright v. dim illumination. This finding is in contrast to an earlier work where a possible phase advance was found in the cortisol rhythm for male volunteers (Brainard et al., 1990). Melatonin showed a dramatic suppression main effect for the bright light group beginning at approximately 2130 hours and continuing to 0630 hours, $F= 39.368$, $p< .0001$. No significant light effects were found for glucose, $F= 1.906$, $p= .198$ and lactate, $F= 1.323$, $p= .277$. Further, there were no significant time of day effects for glucose $F=.308$, $p=.930$ or lactate $F= .099$, $p= .996$. These data show that improvements in cognitive performance associated with bright light exposure are simultaneous with significant changes in oral temperature and melatonin, but not with glucose and lactate. Further studies are needed to clarify the mechanisms associated with bright light exposure, behavioral benefits and physiological change. These findings are of potential value in optimizing environments for individuals with extended work/rest cycles such as civilian shift workers, military personnel and astronauts.

References

Brainard, G., French, J., Hannon, P., Rollag, M., Hanifin, J., and Storm, W. (1991) "The influence of bright illumination on plasma melatonin, prolactin and cortisol rhythms in normal subjects during sustained wakefulness" Sleep Research, 20:444.

Hannon, P., Brainard, G., Gibson, W., French, J., Arnall, D., Brugh, L., Littleman-Crank, C., Fleming, S., and Howell, B. (1991) "Effects of bright illumination on oral temperature and cognitive performance in humans during nighttime hours" Sleep Research, 20:444.

Presented to:
Association of Professional Sleep Societies, June, 1992 meetings.

Oral presentation - June 23, 1991, San Antonio, Texas

EFFECTS OF BRIGHT ILLUMINATION ON SUBLINGUAL TEMPERATURE,
CORTISOL AND COGNITIVE PERFORMANCE IN HUMANS DURING NIGHTTIME
HOURS P. Hannon, G. Brainard, W. Gibson, J. French, D. Arnall, L.
Brugh, C. Littleman Crank, S. Fleming, J. Hanifin and B. Howell,
intr. by G. Brainard, Northern Arizona University, College of
Health Professions, Flagstaff, Az; USAF Sch. Aerospace Med.,
Brooks AFB, Tx, and Jefferson Medical College, Philadelphia, PA.

The objective of this study was to assess the effects of
bright illumination on sublingual temperature, plasma cortisol
and behavioral measures to determine if bright light can reduce
fatigue and enhance human work performance during specific
nighttime periods. **Methods:** Twelve senior Air Force ROTC male
cadets, ages 21-29, were exposed to two lighting conditions in a
counter-balanced design to evaluate a) order of presentation
effects b) time of night effects and c) illumination condition
(bright v. dim) effects across the 5 respective measurement
periods from 0030 hrs through 0800 hrs. On one night, subjects
were exposed to bright illumination (5000 lux Vita-lite, Duro-
test Corp.) from 2100 hrs to 0800 hrs. During the other night,
subjects were exposed to dim illumination (50 lux) throughout the
night. A minimum of two weeks separated these two nights of
experimentation. **Results:** A repeated measures ANOVA showed that
subjects had significantly ($p < 0.001$) higher oral temperature from
2100 hrs to 0800 hrs when exposed to bright v. dim illumination.
Subjects had typical nocturnal rhythms of plasma cortisol with no
significant effects of bright v. dim illumination. Main effects
for the cognitive measures during bright illumination favored
speed and speed x accuracy on 4 of the 29 dependent variables
$p < 0.02$ on the WRPAB. Twenty of the remaining 25 variables
favored bright illumination, but did not meet the required $p < 0.05$
alpha level for statistical significance. These data suggest
human work performance can be enhanced during the night by
exposure to bright light. Supported by Dept. of Defense
Grant(DOD 88450-1384); USAFOSR Grant(AFOSR 89-0164) to PH and
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EFFECTS OF BRIGHT WIDE SPECTRUM ILLUMINATION ON SUBLINGUAL TEMPERATURE AND COGNITIVE PERFORMANCE IN HUMANS DURING NIGHTTIME HOURS

Patrick Hannon, George Brainard, William Gibson, Jonathan French, David Arnall, Lisa Brugh, Cynthia Littleman Crank, Scott Fleming, and Brian Howell
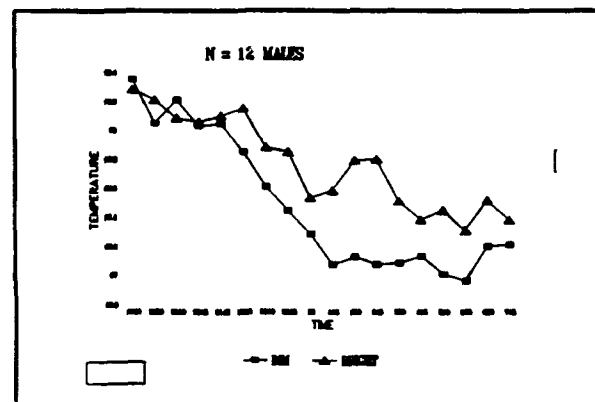Northern Arizona University, USAF Sch. Aerospace Med., Brooks AFB, and Jefferson Medical College

The objective of this study was to assess the effects of wide spectrum, bright illumination upon sublingual temperature and behavioral measures to determine if this illumination treatment can reduce fatigue and enhance human work performance during specific evening and night time periods. Specified illumination levels are typically short term task focused without factoring in possible subtle effects of lighting conditions upon people which may only become apparent after relatively long duration performance on work tasks. This research effort investigated the possibility that human performance may be less than optimal under the 5 to 500 lux light environment that is typical of many work station settings and that a more optimal performance result may be achieved with bright wide spectrum illumination.

Methods: Twelve male subjects, ages 21-29 were recruited from a pool of Senior Officer Cadets enrolled in the Air Force ROTC Program at Northern Arizona University. All subjects were in excellent health with 20/20 or better visual acuity and were "pilot rated". In advance of testing, subjects were instructed to refrain from any medication for 72 hours prior to an experimental/control condition session. Subjects were instructed to avoid all anti-inflammatory and/or pain medication, cold or allergy medication, alcohol, and any beverage containing a stimulant such as caffeine. Further, subjects were asked to eliminate all outdoor recreational activities for a period of 72 hours prior to the experimental/control condition so as to avoid prolonged exposure to sunlight. Finally, subjects were asked to stay up 2 hours past their normal bedtime on the night before each testing night.

Subject preparation began at 1700 hrs with training and stabilization scheduled from 1800 hrs to 2400 hours. A dim baseline illumination (50 lux Vita-lite, Duro-test Corp) was maintained from 1800 hrs through 2100 hrs in both treatment conditions. Subjects were exposed to the 2 lighting conditions in a counter-balanced design (minimum 2 weeks between conditions) to evaluate a) order of presentation effects b) time point effects and c) illumination condition (bright v. dim) effects across the 5 respective measurement periods from 0030 hrs through 0800 hrs. On one night a bright wide spectrum illumination (5000 lux Vita-lite) treatment condition was administered from 2100 hrs to 0800 hrs. The other night maintained the baseline 50 lux illumination condition throughout the night. Sublingual temperature was measured using a Revco Digital thermometer every 45 minutes commencing at 1800 hrs. The test battery of cognitive performance measures were administered every 1.5 hrs and consisted of selected tests from the Walter Reed Performance Assessment Battery (WRPAB) and the Comprehensive Cognitive Assessment Battery (CCAB). The setting consisted of a PC work station under a large 3 articulation light fixture which permitted precise overhead fixture placement for each subject. Social interaction was minimized by testing only one subject each night and by the demands of the protocol.

Results: A repeated measures 3-way ANOVA indicated that the bright wide spectrum illumination better maintained oral temperature from 2100 hrs to 0800 hrs, p <.001 (see Figure 1). Main effects for the cognitive measures were analyzed with a repeated measures 3-way ANOVA. Order of illumination treatment effects were absent for data in both the WRPAB and CCAB. The bright illumination condition favored speed and speed x accuracy on 4 of the 29 dependent variables p< .02 on the WRPAB. Specifically, bright light favored serial addition speed (p=0.001 and code substitution speed (p=0.003) and speed x accuracy (p=0.016). Twenty of the remaining 25 variables favored bright illumination, but did not meet the required p< .05 alpha level for statistical significance. Results for the CCAB also indicated a trend toward a light effect with 66% of the measures favoring bright illumination. None of the CCAB measures were statistically significant at the p< .05 alpha level.

Conclusions: The effect of bright wide spectrum light upon the sublingual temperature circadian marker is pronounced. This relative elevated oral temperature is accompanied by improved performance on some cognitive performance measures from 0030 through 0800 hrs. Work that demands vigilance and is monotonous may be especially sensitive to this lighting variable during nighttime hours. These findings are of potential value in optimizing environments for individuals with extended work/rest cycles such as civilian shift workers, military personnel and astronauts.

BIOLOGICAL EFFECTS OF LIGHT IN HUMANS: THE REGULATION OF PHYSIOLOGY, MOOD AND BEHAVIOR

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Introduction

It is obvious that light entering the eye permits the sensory capacity of vision. The human species is highly dependent on visual perception of the environment and consequently, the scientific study of vision and visual mechanisms is a centuries old endeavor. Relatively new discoveries are now leading to an expanded understanding of the role of light entering the eye - in addition to supporting vision, light has various nonvisual biological effects. Over the past thirty years, animal studies have shown that environmental light is the primary stimulus for regulating circadian rhythms, seasonal cycles, and neuroendocrine responses (1-3). As with all photobiological phenomena, the wavelength, intensity, timing and duration of a light stimulus is important in determining its regulatory influence on the circadian and neuroendocrine systems (4-8). Initially, the effects of light on rhythms and hormones were observed only in sub-human species. Research over the past decade, however, has confirmed that light entering the eyes of humans is a potent stimulus for controlling physiological rhythms (9-12). The aim of this paper is to examine three specific nonvisual responses in humans which are mediated by light entering the eye: light-induced melatonin suppression, light therapy for winter depression, and enhancement of nighttime performance. This will serve as a brief introduction to the growing database which demonstrates how light stimuli can influence physiology, mood and behavior in humans. Such information greatly expands our understanding of the human eye and will ultimately change our use of light in the human environment.

Stimulation of the Circadian and Neuroendocrine Systems by Light

In most vertebrate species, it is known that light enters the eyes and stimulates the retina.
Nerve signals are sent from the retina to the visual centers of the brain and permit the
sensory capacity of vision. In addition, neural signals are sent from the retina into the
hypothalamus, a non-visual part of the brain. The hypothalamus is a complex neural
region that influences or controls many basic functions of the body including hormonal
secretion, core temperature, metabolism and reproduction as well as higher cognitive
functions such as memory and emotions (13). Information about environmental light is
sent from the retina to a specific part of the hypothalamus, the suprachiasmatic nucleus
(SCN) (14, 15). This part of the brain is considered to be a fundamental part of the
"biological clock", or circadian system, which regulates the body's physiological rhythms.
The circadian system is thought to be responsible for controlling daily rhythms such as
sleep and wakefulness, body temperature, hormonal secretion and other physiological
parameters including cognitive function. It is now clear that light is the primary stimulus
for regulating the circadian system, although other external stimuli such as sound,
temperature and social cues may also influence the body's timing functions (1, 2).

The SCN relays retinal information to many of the major control centers in the nervous
system (15). One nerve pathway that carries non-visual information about light extends
from the SCN to the pineal gland via a multisynaptic pathway with connections being made
sequentially in the paraventricular hypothalamus, the upper thoracic intermediolateral cell
column, and the superior cervical ganglion (15, 16). Cycles of light and darkness relayed
by the retina entrain SCN neural activity which, in turn, entrains the rhythmic production
and secretion of melatonin from the pineal. In humans and all other vertebrate species
studied to date, high levels of melatonin are secreted during the night and low levels are
released during the day (2, 3, 9, 17).

The Effects of Light Intensity and Wavelength on Melatonin Suppression

In addition to entraining melatonin secretion from the pineal gland, light can have an acute
suppressive effect on melatonin . Specifically, exposure of the eyes to light during the
night can cause a rapid decrease in the high nocturnal synthesis and secretion of melatonin
(7, 18, 19). Early studies on humans did not demonstrate the acute suppressive influence
of light on plasma melatonin (17, 20-22). However, Lewy and colleagues (9)
demonstrated that exposing the eyes of normal volunteers to 2500 lux of white light during

the night induced an 80% decrease in circulating melatonin within one hour. In contrast, volunteers exposed to 500 lux of white light exhibited no significant melatonin suppression (9). Earlier attempts at suppressing melatonin in humans with light failed when investigators used typical indoor light levels of 100 to 800 lux (17, 20-22). Whereas such typical room light would be sufficient for suppressing melatonin in many animal species (2, 3, 7, 18, 19), and would be adequate for human vision, it was not enough to suppress melatonin in those experiments. Simply put, it takes much more light to suppress melatonin than is required for vision. The discovery that much brighter light is needed to suppress melatonin in humans provided the groundwork for numerous studies on the internal responses of humans to bright artificial light. However, the notion that only "bright" light can drive neuroendocrine and circadian responses is not entirely accurate.

To begin with, the term "bright" refers to a subjective visual sensation and is thus a relative descriptor (23). A 2500 lux light indoors indeed appears "bright" relative to typical indoor levels ranging from 100 to 800 lux. In contrast, 2500 lux of light outdoors is relatively dim compared to daylight at high noon which reaches 100,000 lux (24). Several years after it was discovered that light at 2500 lux can suppress melatonin in humans, a study was done to more precisely determine the dosages of light needed to suppress melatonin in normal volunteers (25). In that study, six normal males were exposed to carefully controlled intensities of monochromatic green light at 509 nm for one hour during the night. Specifically, the volunteers were continuously exposed to the experimental light between 02:00 and 03:00 hours with their pupils fully dilated by a mydriatic agent, their heads held steady relative to the light source by an ophthalmologic head holder, and with translucent white integrating spheres covering both eyes. This procedure produced a constant and uniform illumination of the whole retina during the entire light exposure. The data from this experiment (Figure 1) demonstrated that light affects a human hormone in a dose-response fashion: i.e., the brighter the photic stimulus the greater the suppression of melatonin (25).

It is interesting that all of the stimuli used in this study activated the visual system: both the volunteers and the experimenters saw all the different light intensities and accurately reported them to be green. The lower light intensities, however, did not change hormone levels whereas the higher intensities induced a 60-80% decrease in this hormone. Thus, light that activates vision does not necessarily cause neuroendocrine change. It appears to be generally true in both animals and humans that much more light is needed for biological

effects than for vision. The data shown in Table 1 provide the photometric and radiometric values for the stimuli used in constructing this dose-response function.
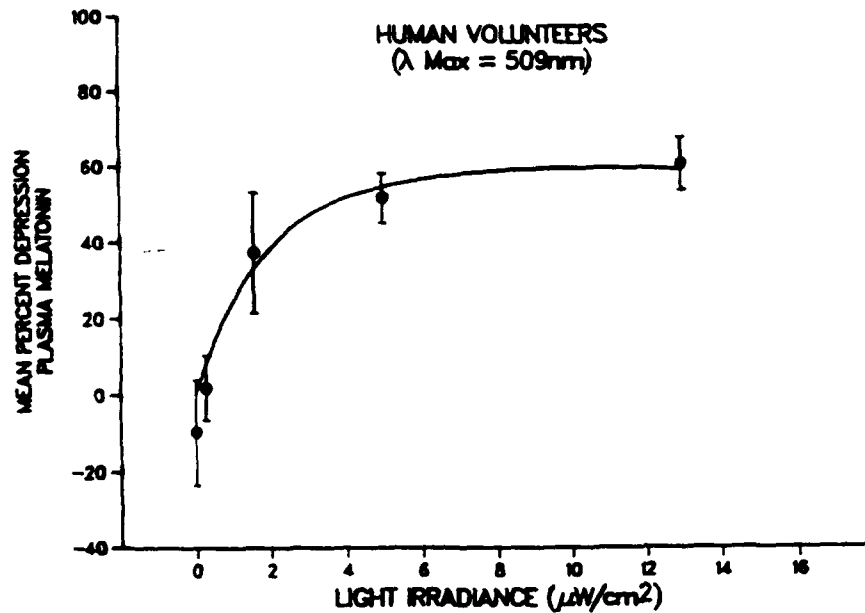

Figure 1: The dose-response relationship between green monochromatic light (509 nm, 10 nm half-peak bandwidth) exposure of normal volunteers eyes and suppression of the hormone melatonin (25). Data points indicate mean ± SEM.

Table 1: Radiometric and Photometric Stimuli Used in the Melatonin Dose-Response Curve (25)

$\mu W/cm^2$	photons/cm^2	photopic lux	scotopic lux	% melatonin suppression
0.01	9.19×10^{13}	0.03	0.17	-9.67
0.3	2.76×10^{15}	1.03	5.25	1.83
1.6	1.47×10^{16}	5.50	27.98	37.33
5.0	4.59×10^{16}	17.18	85.90	51.67
13.0	1.19×10^{17}	44.66	227.37	60.67

The demonstration of the dose-response function for light suppression of melatonin in humans produced an unexpected result: very bright light is not necessarily needed for melatonin suppression. As demonstrated by Table 1, the mean threshold illuminance for suppressing melatonin was between 5 and 17 lux in normal volunteers - a level of

illumination equal to civil twilight and well below typical indoor light. This means that under the proper conditions, 25 to 100 times less light can suppress melatonin than originally thought (9). Why did ambient room light at levels much higher than 17 lux not suppress melatonin in earlier experiments? In those early studies (9, 17, 20-22), neither the exposure conditions nor the light stimuli were optimized. Often the experimental light stimulus consisted of turning on the overhead light provided with the experimental room. In almost any given room, it is possible to vary the light illuminance entering the eyes by a factor of 10 simply by changing the direction of gaze. Thus, in a room characterized as having "typical"-illumination levels of 500 lux, the occupants may be able to see up to 500 lux if they look directly towards the light fixtures, but if they look at the floor or walls, this light reaching their eyes may be as low as 50 lux. Furthermore, the pupil of the eye adjusts dynamically to further restrict the amount of light which reaches the retina. A maximally restricted pupil can reduce the light reaching the retina to as little as one sixteenth of the light falling on the cornea (26). In addition, the amount of the retina exposed to the light stimulus varies greatly with the geometry of the light source and the relative direction of gaze. A recent study by Gaddy and colleagues has shown partial retinal exposure is less effective compared to the whole retinal exposure for suppressing melatonin (27). Finally, the amount of light entering the eye can be further reduced by shadowing of the cornea by the bony orbit, squinting and eye blink. Thus, both behavioral and ocular factors can functionally reduce the amount of light reaching the retina to a level where it is not effective in suppressing melatonin levels. In the early studies, we presume that no efforts were made to control pupil size, direction of gaze, and retinal field exposure since none of these experimental details were reported. Hence, in those experiments "ordinary room levels of illumination" did not suppress melatonin (9, 17, 20-22) and only when much brighter light was used (9) could hormone production be altered. However, it is clear that very low levels of light can indeed suppress melatonin when the exposure factors are optimized (25).

In addition to exposure factors and light intensity being critical in determining if a light stimulus will suppress melatonin, the spectral quality of light is important in determining its relative biological impact. Studies done on the effects of different wavelengths on hamsters, rats and mice suggest that wavelengths in the blue and green portion of the spectrum have the strongest impact on circadian and neuroendocrine regulation (5, 6, 28-38). Some data have supported the hypothesis that the rod photopigment rhodopsin is the primary receptor for circadian and neuroendocrine regulation (5, 6, 28, 33, 34, 36, 37). In contrast, other data have suggested that one or more cone photopigments may be involved in these regulatory effects (28, 33-37). It is important to note that while the highest

sensitivity is in the blue-green range, this does not preclude other wavelengths from participating in circadian and neuroendocrine regulation. For example, in terms of melatonin suppression, short wavelengths in the ultraviolet region of the spectrum (33, 36-38) and longer wavelengths in the red portion of the spectrum are quite capable of suppressing melatonin in rodents if the intensity is sufficiently high (39-41). Further studies are required to conclusively identify what specific photoreceptors and photopigments are involved in regulating the circadian and neuroendocrine systems in animals.

Only one study has specifically examined wavelength regulation of melatonin in humans (25). That study suggested that the peak sensitivity for melatonin suppression is in the blue-green range as seems to be the case in some lower mammals. It is premature, however, to draw any conclusions as to what photoreceptors are involved in any nonvisual physiological regulation in humans.

Use of Light to Treat Winter Depression

While research over the past decade has proceeded on the biological effects of light in humans, concurrent studies have tested the use of light as a therapeutic tool for improving mood and psychological status of patients diagnosed with winter depression. It has been noted since antiquity that some individuals are adversely affected by the changing seasons. More recently, the specific condition of fall and winter depression or Seasonal Affective Disorder (SAD), has been formally described in the scientific literature (42, 43, for reviews: 44-46) and been included in the latest edition of the American Psychiatric Association's diagnostic manual (DSM-III-R, 47). People affected with this malady often experience a dramatic decrease in their physical energy and stamina during the fall and winter months. As daylengths become shorter and temperatures become cooler, individuals with SAD often find it increasingly difficult to meet the demands of life - they can not function well in their jobs or can not cope with everyday family life. In addition to a general decrease in energy, they experience emotional depression and feelings of hopelessness and despair. Other symptoms of winter depression or SAD may include increased sleepiness and need for sleep, increased appetite (particularly for sweets and other carbohydrates), and a general desire to withdraw from society. People afflicted with this malady often feel compromised in meeting the ordinary demands and responsibilities of

everyday life. Fortunately, among those who are accurately diagnosed with SAD, daily light therapy has been found to effectively reduce symptoms in many patients (42-46).

There are now numerous clinics across the United States that offer light therapy for people who are afflicted with winter depression (48, 49). Specific treatment protocols vary somewhat between different clinics. One frequently used procedure involves a patient sitting at a specific distance from a fluorescent light panel which provides a 2500 lux exposure when looking directly at the lamp. The patient is told not to gaze steadily at the bright light, but rather to glance directly at the unit for a few seconds each minute over a two hour period. During the therapy period, a patient may read, watch television, work at a computer or do other hand work. Patients often respond to this therapy after two to seven days of light treatment and continue to benefit as long as the treatment is repeated daily throughout the months that the individual experiences winter depression (43-46).

The white light used for treating SAD can be effectively provided by a range of lamp types including incandescent, cool-white fluorescent, and "sunlight simulating" fluorescent, (42-46, 50-57). Furthermore, there is an assortment of light devices available for treating SAD. Light therapy instruments come in a variety of shapes and configurations including workstations (52), head-mounted light visors (53 - 55) and automatic dawn simulators (56, 57). These devices are configured to shorten therapeutic time, increase patient mobility or to permit therapy during the sleep period. Doubtless there will be continued development, diversification and improvement of light therapy devices and strategies.

- The Effects of Different Wavelengths in SAD Phototherapy

Current evidence supports the hypothesis that light therapy for SAD works by way of light shining into the eyes as opposed to light on the skin (58). It is not known, however, what ocular photoreceptors or photopigments mediate the therapeutic benefits of light in winter depression. To date, three consecutive studies have specifically compared different portions of the spectrum for clinical efficacy in treating SAD (59-61). In the first study, 18 patients were treated with an equal photon dose of white, blue or red light light for a period of one week. The photon dose of 2.3×10^{15} photons/cm^2/sec was selected because this particular photon density of broad spectrum white light (400-760 nm half-peak bandwidth, Vitalite® lamps, Durotest Corp.) had been shown in many previous studies to be clinically effective in one week of therapy (44, 45). The red and blue light sources used in this study

(F40R and F40BB lamps, Westinghouse Div., Philips Inc.) had half-peak bandwidths of approximately 615-685 nm and 430-465 nm, respectively. Patients' clinical status before and after light therapy was followed by means of the 21-item Hamilton Depression Rating Scale (HDRS), a standard scale for measuring symptoms associated with depression (62). The results of this study are illustrated in Figure 2.
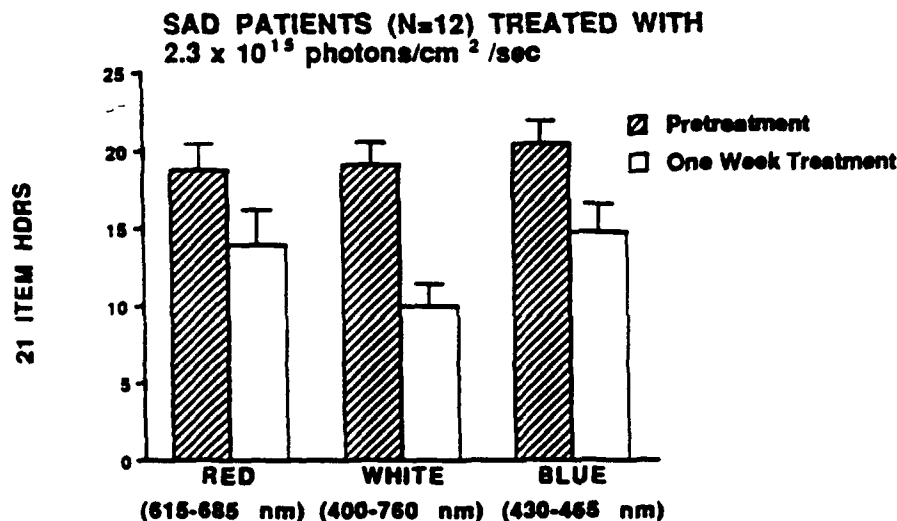

SAD PATIENTS (N=12) TREATED WITH 2.3 x 10^{15} photons/cm² /sec

Figure 2: The bars in this graph indicate mean +SEM Hamilton Depression Rating Scale values for patients before treatment (hatched bars) and after one week of treatment with equal photon densities of different light spectra (open bars). Numbers in parentheses indicate the half-peak bandwidth of the light source (59).

- This study was the first step towards defining an action spectrum of light therapy for winter depression. As shown in Figure 2, one week of light therapy with each of the three light sources produced an improvement in depression symptoms among the groups of patients tested. Specifically, the percent drop in mean HDRS scores were 26%, 47% and 27% for the red, white and blue light sources, respectively. Thus, the photon density emitted from the white light source elicited a significantly stronger clinical response compared to the results obtained from an equal photon density from the blue and red light sources (59). This suggests that broad spectrum white light at this particular photon density is superior to restricted bandwidths of light in the red and blue portions of the visible spectrum. That result implies that light sources for SAD light therapy could not be improved by narrowing the wavelengths provided and shifting them towards either end of the visible spectrum. It is

logical, however, to question the relative efficacy of a green bandwidth of light for treating winter depression.

To resolve that question, a second study was done comparing green light to red light at 2.3 x 10^{15} photons/cm^2/sec for treating SAD (60). The green and red light (F40G and F40R lamps, Westinghouse Div., Philips Inc.) had half-peak bandwidths of approximately 505-555 nm and 615-685 nm, respectively. Patients' clinical status before and after one week of light therapy was followed by means of the 21-item HDRS. The results of this study are illustrated in Figure 3.

SAD PATIENTS (N=14) TREATED WITH
2.3 x 10^{15} photons/cm^2/sec

Figure 3: The bars in this graph indicate mean +SEM HDRS values for patients before treatment (hatched bars) and after one week of treatment with equal photon densities of -green or red light. Numbers in parentheses indicate the half-peak bandwidth of the light source (60).

As illustrated in Figure 3, one week of light therapy with both green and red light sources produced an improvement in depression symptoms in the groups of patients tested. The percent reduction in mean HDRS scores was 51% and 30% for the green and red light sources, respectively. Hence, at this photon density, green light was significantly stronger than the red light for treating winter depression (60). The results of this study (Figure 3) considered alongside the results from the study comparing red, white and blue light therapy at the same photon density (Figure 2) suggest that broad spectrum white light and narrower band green light are equivalent in their capacity to reduce symptoms of SAD. Between the two studies, white and green light treatments were associated with a 48% and

53% reduction in HDRS scores, respectively. Comparisons of group responses between different studies, however, are not conclusive. Are white and green light really equivalent in their phototherapeutic strength?

To answer that question, 12 patients were given one week of light therapy for SAD with either green or white light at an equal photon density (61). Since therapy with white and green light appeared to cause roughly equivalent HDRS reductions across the first two studies, the experimental photon density was lowered to 1.23×10^{15} photons/cm^2/sec in the third study. As in the first two studies, patients' clinical status before and after one week of light therapy was followed by means of the 21-item HDRS. The results of this study are illustrated in Figure 4.

SAD PATIENTS (N=12) TREATED WITH 1.23 x 10^{15} photons/cm^2 /sec
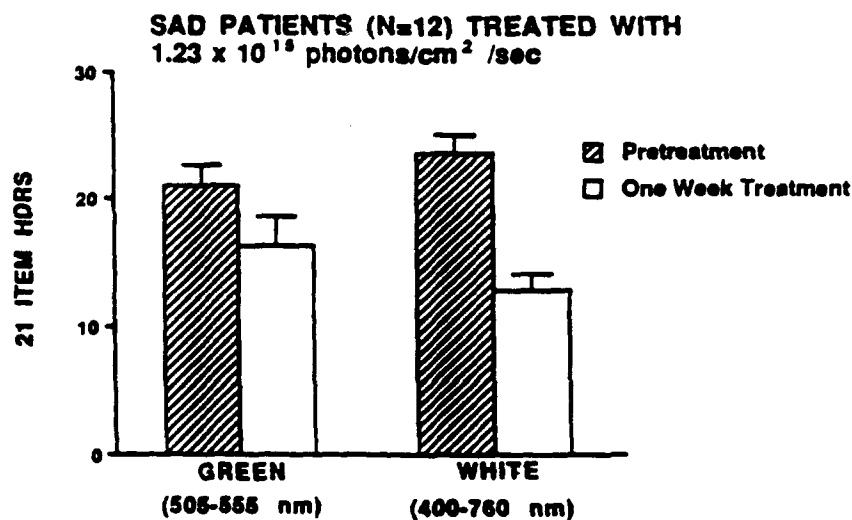

- Figure 4: The bars in this graph indicate HDRS values (mean +SEM) for patients before treatment (hatched bars) and after one week of treatment with equal photon densities of white or green light. Numbers in parentheses indicate the half-peak bandwidth of the light source (61).

As shown in Figure 4, one week of therapy with each of the light sources produced an improvement in depression symptoms. Specifically, the percent drop in mean HDRS scores was 22% for the green light and 46% for the white light sources. At this lower photon density, white light was superior to the green light in treating SAD (61). Hence, in this study, white and green light were not equivalent in their therapeutic efficacy as the preliminary comparison of the data from the first two wavelength studies suggested.

Together, these three studies form the ground work for determining the action spectrum for SAD light therapy (59-61). The traditional approach to defining a complete action spectrum, however, requires substantially more testing (63). A thoroughly defined action spectrum can guide the development of light treatment devices that emit the optimum balance of wavelengths for treating SAD. Furthermore, an action spectrum will yield important information about the photosensory mechanism(s) responsible for the beneficial effects of light therapy. Currently, it is premature to predict what photopigment(s) or photoreceptor(s) mediate the antidepressant effects of light.

A practical issue debated among SAD researchers concerns the role of ultraviolet radiation (UV) in light therapy. Most of the early studies on SAD therapy successfully utilized fluorescent lamps that emitted white light containing a portion of UV wavelengths (44, 45). Those early results erroneously led to the suggestion that UV wavelengths are necessary for successful therapy. The literature, however, shows clearly that SAD symptoms can be reduced by lamps which emit little or no UV (50, 51, 53-55, 59-61, 64). Hence, UV wavelengths do not appear to be necessary for eliciting positive therapeutic results. Does this rule out UV having any role in relieving winter depression? Studies demonstrate that UV wavelengths can regulate seasonal reproduction, melatonin production, and circadian rhythms in some animal species (29-31, 33, 36-38). Furthermore, in normal, healthy humans up to the age of at least 25 years, UV-A can be detected by the visual system (65-67). Although the latest studies show no decrement in therapeutic response when UV is specifically excluded in SAD treatment, they do not demonstrate that UV is totally noncontributory. Whether or not UV wavelengths can contribute to the optimum balance of wavelengths for SAD therapy remains an open question.

The data presented here make it clear that several methodological problems will have to be overcome before further progress can be made in defining an action spectrum for SAD light therapy. One complication for the wavelength studies and nearly all studies on SAD involves the fact that they are done on an outpatient basis. Hence, patient compliance on treatment timing, frequency and duration cannot be closely controlled even with the most cooperative subjects. Furthermore, very small changes in gaze direction and patient position relative to the light source can cause great variability in the amount of light transmitted to the patients' eyes (68, 69). Did patients have different gaze behaviors or different patterns of light useage with the different wavelength light sources? The optimum method of comparing different wavelengths - or any other photic parameter - for SAD therapy is to work with more carefully controlled exposures. As demonstrated in the

melatonin suppression studies, tight control of ocular light exposure permits substantially lower light levels to regulating hormone secretion. Could the general requirement of 2500 lux or more for SAD therapy be a compensation for differences in patient compliance and exposure variables?

Across the three wavelength studies outlined above, each light treatment produced some therapeutic improvements. Does this indicate that each light was at least partially effective in treating SAD symptoms, or are some of the therapeutic benefits of light therapy due to a non-specific or placebo response? Since patient expectations of treatment outcome are thought to contribute significantly to the placebo effect, evaluation of expectations before treatment is one strategy for approaching this question. Prior to any light treatment, subject expectations were systematically probed in each of the three wavelength studies. In general, all subjects had positive expectations about the success of light therapy but there were no differences between the expectations for the different light spectra in these studies (59-61). This evidence supports the idea that some of the therapeutic benefit of the different light spectra may have been due to a placebo response but that the differential therapeutic responses to the different light spectra were not merely an extension of the patients' preconceived beliefs.

In the medical literature it has been well documented that patients with a wide range of disorders - depression, schizophrenia and anxiety as well as cancer, diabetes and ulcers - can successfully respond to inactive or placebo treatments (70, 71). Hence it would be remarkable if SAD patients did not show some level of placebo response to light therapy. In fact, therapeutic improvements are almost always observed with light treatments - regardless of light intensity, wavelength and duration (44-46). Although it is obvious that light therapy indeed will reduce patients' depression symptoms, the critical question is how much of the patients' response to light therapy is due to a non-specific placebo response versus a geniuine clinical response? This remains an open question in the SAD field and has been discussed most insightfully by Eastman (71). Unfortunately, until this question is resolved, a more conclusive action spectrum for SAD phototherapy may not be possible. The inability to accurately separate placebo responses from genuine clinical antidepressant responses causes an element of "noise" in phototherapy data which seriously hinders the accurate discrimination of differential wavelength effects in light therapy.

Use of Light for Enhancing Performance and Treating Problems of Night Workers

Over the past decade, most of the studies on light therapy have been concerned with winter depression. Other research, however, has begun to extend the applications of light therapy. Investigators have had some success in treating certain sleep disorders with phototherapy (72, 73). In addition, studies have indicated that individuals with either non-seasonal depression (50, 74) or pre-menstrual syndrome (PMS) may benefit from light therapy (75, 76). Much more work needs to be done in determining the utility of light for treating these disorders. It appears that we are entering a frontier of medicine in which man's biological response to light is being harnessed to alleviate specific illnesses. Such medical developments have encouraged investigators to explore the possibilities of using light for various domestic or non-medical applications.

One area of study involves the function and dysfunction of the human circadian physiology under more challenging situations. Some preliminary studies have tested the use of strategic light exposure to prevent or ameliorate jet lag (77-79). The preliminary findings are generally positive and some investigators are optimistic that light will be a useful tool for quickly resetting the traveler's internal biological clock and overcoming some of the problems associated with jet travel over multiple time zones. There is a consensus among scientists however, that the data in this field - as of August, 1991 - are preliminary and insufficient for a specific prescription on how to best use light for this modern malady (80).

Shift work may pose problems associated with circadian desynchronization analogous to that found in jet lag (10, 81). Instead of rapidly flying to distant countries, the shift worker stays in one place but may just as suddenly change the time period that he is awake or asleep. By the broadest definition, shift workers are individuals who do not work a standard daytime schedule. Instead, they work nights, evenings, rotating shifts, split shifts or extended shifts. It is estimated that one out of five full time workers in the United States (20 million people) is a shift worker (81).

As Campbell and Dawson have reported (82), the two most common and destructive problems associated with shiftwork are reduced quality of sleep following night work and reduced capacity to maintain alertness while at work. Thus, shift work has drawbacks in increased accidents, decreased production and performance deficits among those who are working at night when the body has a natural tendency to be asleep. Furthermore,

evidence indicates that shift workers have increased health problems including higher risk to cardiovascular disease, gastrointestinal distress, as well as cognitive and emotional problems (10, 81-87). Despite these deleterious effects on worker health and efficiency, the number of people involved in shift work is likely to increase. Researchers believe that poor chronobiological adjustment to a permanent or rotating schedule causes some of these ailments (81). Not all of these problems, however, are solely due to a maladapted biological clock. In addition to a desynchronized circadian system, shift workers generally tend to be chronically sleep deprived and experience domestic stresses that are more or less independent of circadian adaptation (10, 81, 83) Hence, there is no single solution to all of the problems associated with shift work.

On the frontiers of shift work research, some investigators are attempting to develop strategies of light stimulation to improve circadian entrainment and to enhance performance and alertness in night workers. In one study, Czeisler and colleagues simulated a night shift routine in the laboratory and tested both biological adaptation and behavioral performance under different lighting stimuli (88). They found that workers given 7,000 to 12,000 lux of white fluorescent light during their work hours and complete darkness to sleep in during the daylight hours, adapted better biologically and had improved alertness and cognitive performance compared to subjects who worked under 150 lux of light and had no complete darkout for sleeping during the day (88). Other studies on simulated shift work have shown that exposure to bright white fluorescent light at specific times can improve sleep quality, enhance performance and speed the adjustment of the circadian system (80, 82, 84, 85). All of these studies were aimed primarily at finding a means of improving adjustment of the circadian system, sleep quality and performance of the shift worker. This experimental approach requires a minimum of 3 to 5 testing days and, under optimum conditions, even longer test periods to adequately discern circadian and sleep changes.

A different experimental approach has been to examine the immediate effects of light stimuli in a single night of work or during prolonged periods of work. The principal focus of this research has been to determine if bright light stimuli can help sustain alertness without degrading performance.   In a study by French and colleagues (89), healthy young volunteers stayed awake and worked continuously at a computer for 30 hours, taking only short breaks to eat or go to the bathroom. While working under 3,000 lux of white fluorescent light during 18:00 to 06:00 hours, the volunteers exhibited significantly improved behavioral and cognitive performance on selected tasks compared to their own

performance on a separate occasion under 100 lux. In addition to these behavioral effects, there were significant differences in the body temperatures, plasma cortisol levels and plasma melatonin levels in these volunteers under the bright versus dim light condition (89, 90). A similar study done in a separate laboratory has also shown that young men doing night work from 21:00 to 08:00 hours under 5000 lux of white light performed better on selected behavioral tasks versus when they worked under light at 50 lux (91). Again, in this study body temperatures and melatonin levels were significantly influenced by light levels. In these acute studies, it is not clear how light is influencing performance. Could the correlated biological changes in body temperature and hormone levels be directly related to improvement in behavioral tests? Is the circadian system involved in these acute effects of light? Are the acute effects of light due to a "masking" of circadian rhythms? Clearly, further studies are needed to clarify the mechanism(s) by which light enhances performance.

There are many occasions when individuals work through the night on an irregular basis, either by free choice, or by unexpected needs emerging in the home or at work. What are the longer term consequences of a single night of bright light exposure for improving alertness and performance? Will the short term gains of enhanced performance or alertness be offset by a longer term disruption of circadian physiology when the individual returns to a regular schedule? This new research raises many unanswered questions. As with jet lag applications, there is a consensus among scientists - as of September, 1991 - that it is still premature to formulate a set prescription on how to best use light for both short term and long term work applications (80, 81). Much additional work is needed in both laboratory simulations and field tests before the overall consequences of using bright light stimuli can be determined and the optimum lighting strategy can be recommended for the varieties of shift work.

As with research on phototherapy for SAD and other disorders, it should be noted that the studies on using light stimuli to improve problems associated with night work may have complications of placebo responses. Simply put, most volunteers can readily see that a manipulation of light is part of the experiment. In such a circumstance, the investigator runs the distinct risk of finding a placebo reaction to the specific light treatments. There are good experimental strategies which can help address the potential problem of a placebo response and some of them are discussed above. One of the best means to avoid placebo problems in lighting studies is to collect both behavioral and biological data. Whereas behavioral variables and subjective mood states may be quite susceptible to the volunteers'

mental preconceptions, objective biological variables such as circadian rhythms, hormone levels, electrophysiological responses, body temperature, urine volume and the like are much less likely to be directly influenced by a placebo response. Collecting physiological and behavioral measures together can greatly improve the reliablity of data on nonvisual biological effects of light of light.

Conclusion

Experimental research on animals during the past thirty years and on humans in the past decade confirm that light can strongly influence the physiology and behavior of many species. With humans, light is a primary stimulus to the circadian system and can regulate many biochemical and physiological processes in the body. The critical parameters of light intensity and wavelength needed to provide this nonvisual biological stimulation are still under study. In addition to these biological effects of light, a high percentage of patients who suffer from winter depression are responsive to bright light therapy. Other clinical disorders also may be treatable with light stimuli. Further pioneering studies are now examining the use of light to improve performance and ameliorate problems associated with shift work. Taken together, these studies provide the initial database for a frontier in medicine and biology. Beyond therapeutic applications, however, what are the potential consequences of this research?

Modern man has become very sophisticated in the specific use of light in his living and working environment. Currently, building interiors are illuminated for three main purposes: 1) providing light for visual performance; 2) providing light for visual comfort; and 3) providing light for aesthetic appreciation of the environment and its contents (23, 92). The studies discussed here demonstrate that light can also influence human physiology, mood and behavior. These data may be the seeds for a revolution in architectural lighting. It is appropriate to begin exploring ways to incorporate these laboratory results into practical architectural lighting designs. Such designs will need to optimize architectural light for nonvisual biological stimulation as well as follow the traditional guidelines for providing correct visual stimulation and comfort. In the long range, this new design consideration is likely to dramatically alter illumination strategies for homes, factories, offices, schools, hospitals and most interior living spaces.

Acknowledgements

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SECOND ANNUAL CONFERENCE

LIGHT TREATMENT
AND BIOLOGICAL RHYTHMS

Sunday & Monday,
May 13 & 14, 1990
New York, New York

LUX

EFFECTS OF BRIGHT ILLUMINATION ON PLASMA CORTISOL IN NORMAL VOLUNTEERS DURING SUSTAINED PERFORMANCE

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The objective of this study was to determine if ambient illumination could influence plasma cortisol levels in humans who were continuously awake for 30 hours. A counter-balanced, within subjects design was used to compare cortisol in 7 healthy male subjects exposed to dim (100 lux) and bright (3000 lux) white light conditions on separate occasions with at least 2 weeks between treatments. Subjects were recruited from healthy civilian and military personnel who had regular nocturnal sleep patterns. For each of the 2 experimental conditions, subjects arrived at the laboratory at 0800 and had an IV catheter with a heparin lock placed in their forearms for withdrawal of blood samples. Subjects were given a series of behavioral measures from the Complex Cognitive Assessment Battery (CCAB) and the Walter Reed Performance Assessment Battery (WRPAB). From 0800 to 1800, all subjects practiced these performance measures under dim illumination (100 lux). From 1800 until 0600 the next day, performance trials were conducted every 2 hours under the dim or bright light treatment. Blood samples were taken from each volunteer at 1100, 1500, 1700, 1900, 2100, 2300, 0100, 0300, 0500, 0700, 0900 and 1100 hours. All samples were drawn into heparinized tubes, centrifuged at 3000 RPM, divided into aliquots, and frozen at -70 °C until thawed for assay. Cortisol levels were determined by single antibody radioimmunoassay. Data were analyzed by ANOVA and Newman-Keuls test. Subjects under both lighting conditions exhibited mean plasma cortisol levels in the normal range for healthy humans, as well as normal diurnal variations for circulating cortisol. Within these normal ranges, however, there were significant differences in cortisol levels between the dim and bright light treated groups (F=3.209, P<0.01). Other data from this study are reported elsewhere (French et al, Ann. Rev. Chronopharm., in press). Specifically, oral temperature, behavioral response times and cognitive error rates were also significantly different between the bright and dim light treated groups. These findings are of potential value in optimizing environments for individuals with extended work/rest cycles such as civilian shift workers, military personnel and astronauts. This work was supported by the USAF School of Aerospace Medicine, USES summer fellowship to PH, and NASA Grant NAGW1196 to GCB.

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Pineal melatonin suppression in rats with electroluminescent light

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(Neurology, Je ..erson Medical College)

To optimize environmental lighting for animals onboard space vehicles, we evaluated a
novel illumination source for its versatility and influence on melatonin suppression. A
flat, electoluminescent panel (3 x 8 inches) was installed on one wall of a 4.5 x 4.5 x 8.5
inch black plexiglass chamber. The electroluminescent light was broad-band white (400
to 740 nm, peak wavelength 510 nm). Intensity was varied with neutral density filters.
Adult male Sprague Dawley rats (64) were entrained to a 12:12 light:dark cycle at least 3
weeks before the experiment under typical fluorescent laboratory lighting. Between 5 and
8 hours into the dark cycle, animals were exposed to electroluminescent light at 55, 4.4,
0.5 or 0.03 $\mu W/cm^2$ in the chamber for 5 minutes. After light exposure, the animals
were held in darkness for 15 minutes before sacrifice. Pineal glands were removed
immediately, frozen on dry ice, and assayed for melatonin content by RIA. Control
animals were handled similarly but not exposed to electroluminescent light. Data were
analyzed for significance by Student's t-test. Animals exposed to 55, 4.4 and 0.5
$\mu W/cm^2$ showed a significant melatonin suppression ($p < 0.001$, 0.001, and 0.005,
respectively). Percent melatonin suppression versus intensity indicated a dose-response
relationship. This experiment demonstrates that illumination from electroluminescent
panels can regulate at least one component of the neuroendocrine system. The light
source may be useful for animal research aboard the unmanned space lab, space shuttle,
and space station. Technically, electroluminescent panels are flat, lightweight and likely
to withstand the vibration and stresses of space travel making them a potentially superior
lighting source for animal habitats in space.

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THE INFLUENCE OF BRIGHT ILLUMINATION ON PLASMA MELATONIN, PROLACTIN AND CORTISOL RHYTHMS IN NORMAL SUBJECTS DURING SUSTAINED WAKEFULNESS
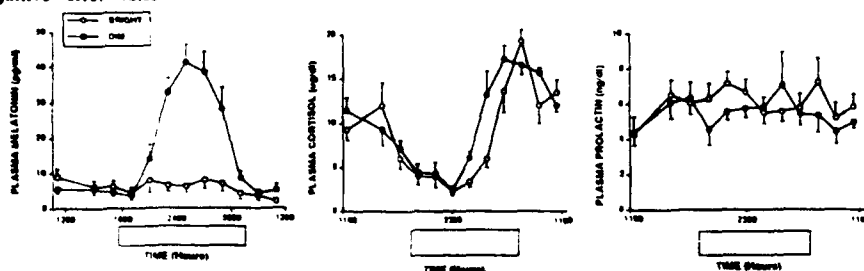
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In laboratory studies, bright light exposure has been associated with improvements in nighttime alertness and performance among night workers[1-4]. Before using bright light stimuli in the work place, it is important to determine how such light exposure influences the neuroendocrine and circadian systems of workers. The objective of this study was to determine the effect of bright light exposure on hormonal rhythms in humans who were continuously awake and working for 30 hours.
METHODS A counter-balanced, within subjects design was used to compare hormone levels in 7 healthy male subjects exposed to dim (100 lux) and bright (3000 lux) white light conditions on separate occasions with at least 2 weeks between treatments. Subjects were recruited from civilian and military personnel who had regular nocturnal sleep patterns. For each of the 2 experimental conditions, subjects arrived at the laboratory at 0800 and had an I.V. catheter with a heparin lock placed in their forearms for withdrawal of blood samples. Subjects were given a series of behavioral measures from the Complex Cognitive Assessment Battery (CCAB) and the Walter Reed Performance Assessment Battery (WRPAB). From 0800 to 1800, all subjects practiced these performance measures under dim illumination (100 lux). From 1800 until 0600 the next day, performance trials were conducted every 2 hours under the dim or bright light treatment. Blood samples were taken from each volunteer at 1100, 1500, 1700, 1900, 2100, 2300, 0100, 0300, 0500, 0700, 0900 and 1100 hours. Plasma melatonin, prolactin and cortisol levels were determined by radioimmunoassay. Data were analyzed by two-way ANOVA.
RESULTS Mean (+/- SEM) hormone concentrations are shown in the graphs below. For plasma melatonin, there were significant main effects of both light intensity (F=16.28, df=1,5, p<0.01) and time (F= 19.23, df=11,55, p<0.001) as well as a significant interaction (F=17.82, df=11,55, p<0.001). For plasma cortisol, there was no main effect of light (F=3.84, df=1,5), but there was a significant main effect of time (F=7.38, df= 11,55, p<0.001) and a significant interaction (F= 2.12, df= 11,55, p<0.05). For plasma prolactin, there was neither a significant main effect of light (F=0.63, df=1,5), nor a significant interaction (F=1.08, df=11,55), but there was a significant main effect of time (F=5.17, df=11,55, p<0.001). As reported elsewhere[1], bright illumination reduced the nocturnal drop in oral temperature and significantly improved volunteers' behavioral response times and cognitive error rates.

CONCLUSIONS Bright light exposure had a profound effect on volunteers' melatonin rhythm and a small, but significant effect on the cortisol rhythm in this study. In contrast, bright light had no apparent effect on prolactin. Extended work/rest cycles are increasingly common for civilian shift workers, military personnel and astronauts. If lighting manipulations are used for improving the performance of night workers, careful attention should be paid to the long and short term hormonal consequences of these lighting changes.

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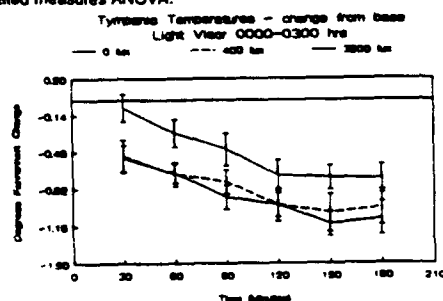## EFFECT OF LIGHT INTENSITY ON ORAL, RECTAL, AND TYMPANIC TEMPERATURE AND FULL BODY ACTIVITY

Mitchell I. Edelson, Sean P. Timey, James R. Gaddy, Karen T. Stewart, and George C. Brainard
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Bright environmental illumination can be a major factor in regulating circadian rhythms and can shift the phase of the human circadian temperature rhythm. Recent studies have shown that exposure to bright light during the night acutely attenuates the normal nocturnal drop in body temperature. French et al. found that exposure to bright light (3000 lux) significantly elevated oral temperature relative to dim light (100 lux) at 2130, 0130, and 0330 hours.[1] Badia et al. also recently observed that nocturnal tympanic temperature decreased more rapidly under dim light (< 50 lux) than bright light (6000-10,000 lux) from 2400 to 0900 hours.[2] To date the effect of light on body temperature has only been tested with light boxes or remote light sources. The present study was designed to determine the intensity from a head-mounted light visor that significantly prevents the nocturnal drop in body temperature.

Subjects and Procedures: A counter-balanced, within subjects design was used to compare oral, rectal, and tympanic temperature in fourteen healthy male subjects with regular nocturnal sleep patterns exposed to 0, 400, and 3200 lux via a light weight, head-mounted light visor (Bio Brite, Inc.) on three different occasions separated by at least one week. The visor illumination was broadband white light (400-750 nm) produced by incandescent Krypton lamps. Mean distance between subject's eyes and light source was 6.5 cm. Major adjustments in illuminance were achieved with neutral density filters. Rectal temperature was recorded via an indwelling, sterile, disposable probe, while tympanic temperature was measured using a FirstTemp tympanic probe. Subjects wore a light visor from 2400 to 0300 hours while watching a videotape on a television screen emitting no more than 3 lux at the film's brightest moment. Oral, rectal, and tympanic temperatures were measured every half hour. Eight out of the fourteen subjects also wore a wrist activity monitor (Actigraph) to measure body movements during the procedure. Activity counts were collected in one minute bins, and both temperature and activity data were analyzed by a repeated measures ANOVA.

Results: The figure shows the mean (+/- 1 S.E.M.) change in tympanic temperature from baseline over 180 minutes for each of the three light intensities. Compared to 0 and 400 lux exposure, 3200 lux significantly prevents tympanic temperature from dropping, $F_{(2,26)}$ = 5.95, p <.01. A similar pattern was observed for rectal temperature that did not reach statistical significance, $F_{(2,26)}$ = 2.49, p= 0.1. Sublingual temperature under different light exposures was not significantly different over the 180 minutes. Body movements in the eight subjects wearing activity monitors showed no significant correlation with body temperature (all r's ≤ 0.65), and did not vary with light intensity, $F_{(2, 14)}$ = 1.04, p=0.4.

Tympanic Temperatures – change from base
Light Visor 0000-0300 hrs

Conclusions: In normal subjects, exposure to bright light (3200 lux) via a light visor during the night appears to significantly elevate tympanic temperature in comparison to no light and dim light. The higher tympanic temperatures cannot be attributed to an increase in general activity since activity did not vary with temperature.

[1]French, J., Hannon, P., and Brainard, G.C. (1990) Ann. Rev. Chronopharmacology, 7:37-40.
[2]Badia, P. et al. (1990) Sleep Research, 19:386.

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EFFECTS OF BRIGHT ILLUMINATION ON ORAL TEMPERATURE
AND COGNITIVE PERFORMANCE IN HUMANS DURING NIGHTTIME HOURS

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The objective of this study was to compare the effects of bright and dim illumination on sublingual temperature and behavioral measures to determine if illumination treatment can reduce fatigue and enhance human work performance during specific evening and nighttime periods. Lighting levels for work are typically task specified for actual optimal visual stimulation without considering potential biological and behavioral effects of the light stimuli. This research effort investigated the possibility that human performance may be less than optimal under the 50 to 500 lux light environment that is typical of many work station settings and that performance may be improved under bright wide spectrum illumination.

Methods: Twelve healthy "pilot rated" male subjects, ages 21-29 were recruited from Senior Officer Cadets enrolled in the Air Force ROTC Program at Northern Arizona University. Subjects were instructed to refrain from all medications, alcohol, and caffeine stimulants for 72 hours prior to an experimental session. Finally, subjects were asked to stay up 2 hours past their normal bedtime on the night before each testing night. Subjects awoke between 0600 and 0700 hrs the day of testing and spent the entire day awake before reporting to the laboratory at 1700 hrs.

Subject preparation began at 1700 hrs with training and stabilization scheduled from 1800 hrs to 2400 hours. A dim baseline illumination (50 lux Vita-lite, Duro-test Corp.) was maintained from 1800 hrs through 2100 hrs in both treatment conditions. Subjects were exposed to the 2 lighting conditions in a counterbalanced design (minimum 2 weeks between conditions) to evaluate a) order of presentation effects b) time point effects and c) illumination condition (bright v. dim) effects across the 5 respective measurement periods from 0030 hrs through 0800 hrs. On one night, subjects were exposed to bright wide spectrum illumination (5000 lux Vita-lite) from 2100 hrs to 0800 hrs. On the other night, subjects were exposed to the 50 lux illumination condition throughout the night. Sublingual temperature was measured using a Revco Digital thermometer every 45 minutes commencing at 1800 hrs. The test battery of cognitive performance measures were administered every 1.5 hrs and consisted of selected tests from the Walter Reed Performance Assessment Battery (WRPAB) and the Complex Cognitive Assessment Battery (CCAB). The setting consisted of a PC work station under a large 3 articulation light fixture which permitted precise overhead fixture placement for each subject. Social interaction was minimized by testing only one subject each night and by the demands of the experimental protocol.

Results: A repeated measures 3-way ANOVA indicated that subjects' oral temperatures were significantly higher during exposure to bright light compared to dim light from 2100 hrs to 0800 hrs, $p < .001$ (see Figure below). Main effects for the cognitive measures were analyzed with a repeated measures 3-way ANOVA. Order of illumination treatment effects were absent for data in both the WRPAB and CCAB. The bright illumination condition favored speed and speed x accuracy on 4 of the 29 dependent variables $p < .02$ on the WRPAB. Specifically, bright light favored serial addition speed ($p = .001$) and speed x accuracy ($p = .001$) and code substitution speed ($p = .003$) and speed x accuracy ($p = .016$). Twenty of the remaining 25 variables favored bright illumination, but did not meet the required $p < .05$ alpha level for statistical significance. Results for the CCAB also indicated a trend toward a light effect with 66% of the measures favoring bright illumination. None of the CCAB measures were statistically significant at the $p < .05$ alpha level.

Conclusions: The effect of bright wide spectrum light upon the sublingual temperature circadian marker is pronounced. This relative elevated oral temperature is accompanied by improved performance on some cognitive performance measures from 0030 through 0800 hrs. Work that demands vigilance and is monotonous may be especially sensitive to lighting effects during nighttime hours. These findings are of potential value in optimizing environments for individuals with extended work/rest cycles such as civilian shift workers, military personnel and astronauts.

DIFFERENTIAL MELATONIN SUPPRESSION DESPITE EQUAL CORNEAL ILLUMINANCE

James Gaddy, Mitchell Edelson, Karen Stewart, Mark Rollag[*] & George Brainard
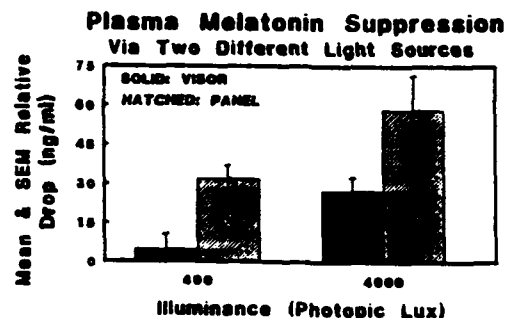Jefferson Medical College, Philadelphia & [*]USUHS, Bethesda

Corneal illuminance (as photopic lux), is often thought predictive of non-visual effects of light including melatonin suppression, circadian rhythm phase shifting and antidepressant activity. We tested this assumption by measuring the effects upon plasma melatonin of two very different light sources equilibrated by photopic lux at the cornea. One source was a 2 x 4 ft fixture with 6 Vita-Lite fluorescent lamps, the other a light visor with two krypton incandescent lamps.

On three nights separated by at least a week, subjects spent from midnight until 0200 hrs in dim light (< 10 lux). On control nights, they remained in this lighting until 0330 hrs. Visor or light panel exposure began at 0200 hrs on the other 2 nights, and continued until 0330 hrs, with the treatment order counterbalanced across subjects. Subjects sat approximately 18 in from the light panel and stared straight into it. The light visor was adjusted so that the subject could sit erect and gaze straight ahead beneath the rim of the visor. One group of 8 male subjects was exposed to an illuminance of 400 lux for both visor and panel and another like group to 4000 lux. Illuminance level was set with neutral density filters for the both sources and also by slight voltage adjustments on the visor.

Plasma samples were taken just before 0200 hrs and at 0330 hrs in all conditions and were assayed for melatonin levels. The change in plasma melatonin was computed for the three conditions for each subject. Experimental effects were normalized for each subject by subtracting control change scores from light exposure change scores. The resulting relative melatonin suppression scores were subjected to ANOVA to evaluate illuminance and light source effects.

Results are shown at right. The panel proved to be more effective in suppressing melatonin than did the visor ($F(1,13)=19.3; p=.001$). The higher illuminance level produced a greater degree of suppression ($F(1,13)=8.08; p=.014$). However, the two light sources were not significantly different in increasing suppression by increasing illuminance (Interaction: $F(1,13)=0.09; p>.05$).

Plasma Melatonin Suppression Via Two Different Light Sources

These results demonstrate that a measurement of corneal illuminance is insufficient to predict the effects of light upon melatonin suppression. Although both the light sources used in the present experiment provided equivalent corneal illuminance, their effects upon plasma melatonin suppression were clearly different. The two light sources differed in both color temperature and area of retinal illumination. Although the precise contribution of these factors to our data cannot be separated, we currently attribute the bulk of it to differences in area of retinal illumination. If further study substantiates this interpretation, it may imply that "dosage" control in therapeutic light exposure will require attention to light source size, source-to-subject distance, and source-to-subject angle, all of which interact to define the area of retinal exposure.

19th Annual Meeting of the American Society for Photobiology

ABSTRACTS OF PAPERS

San Antonio, Texas, 22–26 June 1991

EFFECTS OF BRIGHT ILLUMINATION ON SUBLINGUAL TEMPERATURE, CORTISOL AND COGNITIVE PERFORMANCE IN HUMANS DURING NIGHTTIME HOURS P. Hannon, G. Brainard, W. Gibson, J. French, D. Arnall, L. Brugh, C. Littleman Crank, S. Fleming, J. Hanifin and B. Howell, intr. by G. Brainard, Northern Arizona University, College of Health Professions, Flagstaff, Az; USAF Sch. Aerospace Med., Brooks A.B, Tx, and Jefferson Medical College, Philadelphia, PA.

The objective of this study was to assess the effects of bright illumination on sublingual temperature, plasma cortisol and behavioral measures to determine if bright light can reduce fatigue and enhance human work performance during specific nighttime periods. Methods: Twelve senior Air Force ROTC male cadets, ages 21-29, were exposed to two lighting conditions in a counter-balanced design to evaluate a) order of presentation effects b) time of night effects and c) illumination condition (bright v. dim) effects across the 5 respective measurement periods from 0030 hrs through 0800 hrs. On one night, subjects were exposed to bright illumination(5000 lux Vita-lite, Duro-test Corp.) from 2100 hrs to 0800 hrs. During the other night, subjects were exposed to dim illumination (50 lux) throughout the night. A minimum of two weeks separated these two nights of experimentation. Results: A repeated measures ANOVA showed that subjects had significantly ($p<0.001$) higher oral temperature from 2100 hrs to 0800 hrs when exposed to bright v. dim illumination. Subjects had typical nocturnal rhythms of plasma cortisol with no significant effects of bright v. dim illumination. Main effects for the cognitive measures during bright illumination favored four of the 29 dependent variables $p<0.02$ on the WRPAB. Twenty of the remaining 25 variables favored bright illumination, but did not meet the required $p<0.05$ alpha level for statistical significance. These data suggest human work performance can be enhanced during the night by exposure to bright light. Supported by Dept. of Defense Grant(DOD 88450-1384); USAFOSR Grant(AFOSR 89-0164) to PH and NASA Grant(NAGW 1196) to GCB.

POSSIBLE RETINAL SPATIAL SUMMATION IN MELATONIN SUPPRESSION

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Study of the light perception threshold in classical psychophysics has revealed that retinal sensitivity to light is dependent upon source luminance and wavelength, pupil size, area of retinal illuminance and position of the source image on the retina. Parameters determining retinal sensitivity for the non-visual effects of light such as plasma melatonin suppression, circadian rhythm phase and amplitude shifts and amelioration of major depression have not yet been explored so fully. Although evidence exists for an effect of source luminance (indirectly measured as corneal illuminance), there has been little exploration of the other principle parameters of interest. In order to test the importance of area of retinal illumination, we exposed male subjects in their third decade to light from a head-mounted source which illuminated approximately the lower half of both retinas or to a light panel which illuminated approximately the full retina. While the active treatments were corneal illuminances of 400 or 4000 lux, the control condition was less than 10 lux. Exposure of only the lower half of the retina to the 4000 lux corneal illuminance produced a 27% drop in plasma melatonin levels compared to control conditions while exposure of the most of the retina produced a 97% drop. The 400 lux corneal illuminance produced a 13% drop with the smaller area and a 54% drop with the larger one. Mixed design ANOVA showed both illuminance and area effects to be statistically significant.

PHOTIC PARAMETERS THAT REGULATE THE NEUROENDOCRINE SYSTEM
AND INFLUENCE BEHAVIOR IN HUMANS AND ANIMALS. George C. Brainard,
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In addition to stimulating the sensory capacity of vision, environmental light perceived
by the retina is responsible for entraining circadian rhythms, regulating reproductive
cycles, and influencing a variety of endocrine and metabolic functions in a wide range of
mammalian species including humans. Many of these effects of light are regulated by
retinal pathways not involved in conscious visual perception. The circadian and
neuroendocrine effects of light seem to be principally mediated by the retinohypothalamic
pathway which originates in the retina and terminates in the suprachiasmatic nuclei
(SCN). The main physical parameters which determine whether or not a photic stimulus
will elicit a circadian or neuroendocrine response include light irradiance, wavelength,
exposure duration, time of exposure and presentation method. This review will address
how some of these physical parameters of light influence specific circadian and
neuroendocrine responses. Among the responses considered will be photoperiodic
reproductive physiology of rodents, melatonin regulation in rodents and humans, the
clinical use of light therapy in Seasonal Affective Disorder (SAD), and the use of light to
influence biological adaptation and enhance performance of night workers. Each of these
responses appears to depend on the irradiance and wavelength of photic stimuli as is the
case with all genuine photobiological phenomenon. Supported by the Lighting Research
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BRIGHT LIGHT EFFECTS ON MELATONIN AND COGNITIVE PERFORMANCE.

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RHYTHM

The circadian pulse of the pineal hormone melatonin may be associated with increased sleepiness in humans. Plasma levels of the pineal hormone melatonin are greatest during the sleep phase of the human sleep/wake cycle. Orally administered melatonin is associated with increased subjective indications of fatigue. It is known that nocturnal plasma melatonin levels can be acutely suppressed by bright, white light. The present study concerned the effects of melatonin suppression, using increased light intensity, on nocturnal fatigue degraded performance.

A counter-balanced, within subjects design compared 9 male subjects exposed to dim (100 lux) and bright (3000 lux) light conditions between 1800 and 0600 during a 30 hour sleep deprivation study. Normal nocturnal melatonin levels were suppressed by bright light treatment. Oral temperature was greater and rate of eyeblink was less for the bright light condition compared to the dim light condition. Scores on computer generated cognitive tasks were improved during the bright light exposure, particularly between 0000 and 0400 hours, compared to the dim light. The physiological and performance data suggest that bright light suppression of melatonin attenuated nocturnal performance degradation. In a companion study, bright light was effective in suppressing salivary levels of melatonin. spirer

IS CORRELATED wi

The findings suggest that bright lights, may be used to help sustain night time cognitive ability susceptible to fatigue. Such findings may have important implications for shift worker lighting arrangements. As well, the correlation between salivary and plasma melatonin might lead to the development of a simple non-invasive means to evaluate melatonin circadian cycles.

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BRIGHT LIGHT SUPPRESSES MELATONIN AND IMPROVES COGNITIVE PERFORMANCE DURING NIGHTTIME HOURS IN HUMANS P Hannon*, G Brainard, R Childs, W Gibson, J French, J Hanifin and M Rollag. Northern Arizona University, Coll. of Health Prof., Flagstaff, AZ.,86011; Armstrong Laboratory/CFTO-Brooks AFB, Jefferson Medical College, and Uniformed Services University-Health Sciences.

This study assessed the effects of bright light on biological and behavioral measures to determine if bright light can reduce fatigue and enhance human work performance. Female subjects (N=37) were exposed to one of 3 lighting conditions in a between groups research design. Subjects in the bright light groups were exposed to 5000 lux white light from 1800 hrs to 2400 hrs (Early Bright) or from 2400-0600 hrs (Late Bright). The third group of subjects received 50 lux of red light from 1800-0600 hrs (Dim Red). Blood samples were taken every 90 minutes. Repeated measures ANOVA indicated a significant interaction effect (light x time) for tympanic temperature, ($F=3.339$, $p=.001$). The bright light conditions maintained higher tympanic temperatures from 2300 hrs through 0400 hrs. Plasma melatonin measures indicated a main effects difference of $F=4.009$, $p=.029$. Most importantly, the results showed that the "light" x "time of night" interaction was significant at $F=59.436$, $p=.000$. The suppression of plasma melatonin was greatest from 2230 hrs through 0500 hrs in the Early Bright and Late Bright groups. Cortisol was not affected by the ambient lighting conditions. Dim red light resulted in higher scores on the Stanford Sleep Scale from 2400 hrs through 0500 hrs (light x time, $F= 2.595$, $p=.023$). Subjects under the bright light conditions performed better on the cognitive measures of Code Substitution accuracy ($F= 3.918$, $p=.030$) and Column Addition accuracy ($F=4.660$, $p=.017$). These data show some improvements in cognitive performance and alertness associated with bright light exposure and occur with changes in tympanic temperature and plasma melatonin at critical time periods.

KEY WORDS: (see instructions p. 4)

1. Circadian ___ Temperature
2. Melatonin

PHOTIC EFFECTS ON SUSTAINED PERFORMANCE

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ABSTRACT

The advent of space exploration requires attention to the adaptability of human circadian rhythms in the unique environment of space. Circadian disruption, related to altered sleep work cycles and accelerated solar clues, can lead to fatigue that may impede mission success particularly as the duration of space flights increase. Research is described which evaluates manipulating environmental light intensity as a means to attenuate nocturnal fatigue.

A counter-balanced, within subjects design was used to compare 9 male subjects exposed to dim (100 lux) and bright (3000 lux) light conditions. Oral temperature values were greater for the bright light group over the dim light condition. Melatonin levels were suppressed by bright light treatment. Also, the frequency of eye blink rate was less for subjects during bright over dim light exposure. Light exposure was without effect on subjective fatigue. However, irrespective of light condition, significant effects on confusion, fatigue and vigor mood dimensions were found as a result of 30 hr sleep deprivation. The findings suggest that bright lights, may be used to help sustain nocturnal activity otherwise susceptible to fatigue. Such findings may have implications for the lighting arrangements on space flights during the subjective night for astronauts.

Key Words: Light, Temperature, Melatonin, Performance, Eyeblink, Mood

INTRODUCTION

Acclimatization to extraterrestrial environments represents a challenge to human productivity during future space missions. As extended flights become more frequent, a greater demand on the sustained vigilance of the crew increases the likelihood of performance problems associated with cumulative fatigue. Disrupted sleep is reported to be a common difficulty on shuttle flights particularly when dual shifts are required (Santy, et al., 1988). Fatigue problems related to alterations in circadian sleep work cycles and from unfamiliar light and dark solar cues have been known for some time and have been termed desynchronosis (Winget, et al., 1984). Although most astronauts quickly adjust to the demands of new work shifts in space, some never do and become chronically fatigued (Graeber, 1987). It may be that this fatigue results from an inability to resynchronize to the new circadian work rest cycles required in orbit. Light may serve as an adaptive counter measure for pre-shifting astronauts.

The adaptive characteristics of the circadian cycle to the unique environment of space is relatively unknown. Phase shifting of the sleep cycle as a result of travel across time zones on the earth can produce changes in the topography of the normal sleep EEG (Endo, et al., 1985) that may account for the inadequacy of the rest experienced during orbit. The fatigue produced by circadian disruption can be studied on earth albeit in the absence of microgravity. Effective treatment for fatigue related to circadian disruption may improve the potential for a successful mission. The present study evaluated the effects of ambient light as a counter measure to human fatigue degraded performance and may serve as a model of inducing circadian dysrhythmia.

Recent evidence supports a relationship between environmental light and improved nocturnal alertness (Campbell, et al., 1990, French, et al., 1990). The effectiveness of light exposure on performance enhancement is hypothesized to be related to the ability of light to attenuate the normal nocturnal surge of the pineal hormone melatonin. In support of this hypothesis, many studies suggest that melatonin acts as an endogenous sleep enhancing substance. For example, human subjects given relatively low doses (2 mg) of melatonin for three weeks experienced increased fatigue (Arendt, et al., 1984). Similarly, Lieberman, et al., (1985) using an acute oral dose of

240 mg of melatonin found reduced vigor, elevated fatigue, increased confusion and slowed reaction time. Additionally, plasma levels of melatonin are greatest during the sleep phase of the human circadian cycle. Orally administered melatonin has also been found to alleviate transcontinental disruption of circadian sleep wake cycles (Petrie, et al., 1989). Further, melatonin has a high affinity for receptor sites in the suprachiasmatic nucleus (SCN) of the hypothalamus where it is purported to trigger hormonal entrainment and regulate circadian and circannual rhythms (Reppert, et al., 1988; Brainard, et al., 1988).

Bright, light acutely suppresses plasma melatonin levels in animals (Benshoff, et al.,1987; Brainard, et al.,1982) including humans (Lewy, et al., 1980). The current study addressed the consequences of melatonin suppression via elevated ambient light intensity on temperature, melatonin levels, cognitive abilities, eye blink rate as measured by the electroogulogram and subjective mood.

METHODS

A counter-balanced, within subjects analysis of variance design was used to compare 9 male subjects exposed to dim (100 lux) and bright (3000 lux) conditions. Subjects were recruited from non-smoking civilian and military personnel who indicated a normal nocturnal sleep pattern. During both conditions, scores on cognitive performance tests developed for military human performance labs (Hegge, et al., 1985) were obtained every 2 hours throughout the 30 hour testing session. Beginning at 0600, subjects were stabilized on the performance measures under dim light training conditions. Then at 1800, the light treatment (either dim or bright) began and continued until 0600 the next day. Finally, dim illumination was used until the completion of the experiment at 1200.

Immediately after each performance trial, oral temperature was measured and plasma samples were obtained for later melatonin assays (Brainard, et al., 1991). Monopolar electrodes attached to the bony orbit of the left eye and referenced to the pinna of the left ear were used to determine the blink rate for each subject during a 2 minute recording session, which also followed the performance trial. Blink rate per minute was then visually appraised from 1 minute of artifact free record in a blinded manner. Subjects completed profile of mood surveys (POMS) every 4 hours. They were then allowed 2 weeks before exposure to the second light condition. Subjects were prevented from drinking any caffeinated beverages and were fed the same foods (crackers, chips, sandwiches, fruit, pizza, milk, water, juices) at the same times during each light session.

Five subjects were evaluated at a time during each light session Each subject was assigned to a testing booth that contained a wide spectrum Vita-Light fluorescent lamp (Duro-test Corp., Fairfield, N.J., 07007 Part # 1157030) as the adjustable illumination source and a PC workstation. Each booth was separated from adjacent booths by sound attenuating, frame partitions that restricted the subject's view to their individual workstation. A comfortable chair allowed the subject to sit close to a work table that contained the workstation. The light source was mounted on a wooden frame over the workstation and suspended from an adjustable height to provide directed illuminance within either the dim or the bright treatment ranges. The subjects required to stay in the booth throughout the study with the exception of short (< 10 minute restroom breaks). Social interaction was kept to a minimum between subjects by the experimenter and by the demands of the testing schedule. Dependent measures on the cognitive tasks consisted of response time and accuracy variables. The order that the tests were presented did not vary throughout the study. The 10 performance tests used consisted of the choice reaction time (CRT), column addition and subtraction (CAS), the manikin test (MT), serial addition and subtraction (SAS) and Wilkinson reaction time (WRT). A subjective mood survey was also taken. As well, a tower puzzle (TP), following directions (FD), the numbers (N) and words (W) dual process task and route planning (RP) tests were used.

RESULTS

Oral temperature levels were significantly elevated in the bright light condition compared to the dim light condition at the 2130, 0130 and the 0330 sample points ($p < .05$) as shown in Fig. 1. Subjects in constant dim light had typically low levels of melatonin during daytime and higher levels at night. In contrast, this melatonin rhythm was suppressed by the bright light condition (Figure 2).
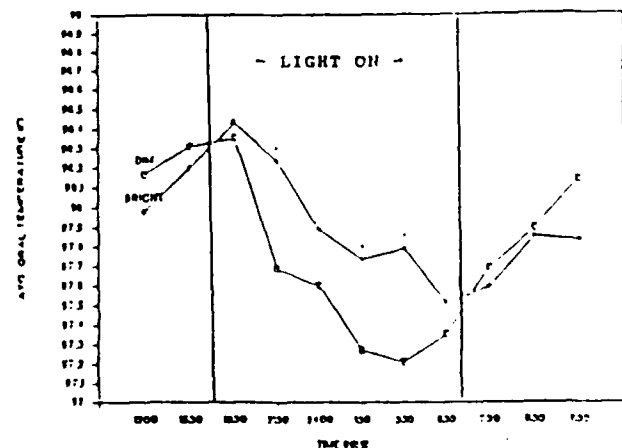

Figure 1. The effect of bright light on oral temperature The onset of the bright light is indicated and differences from the dim light condition are marked with an *
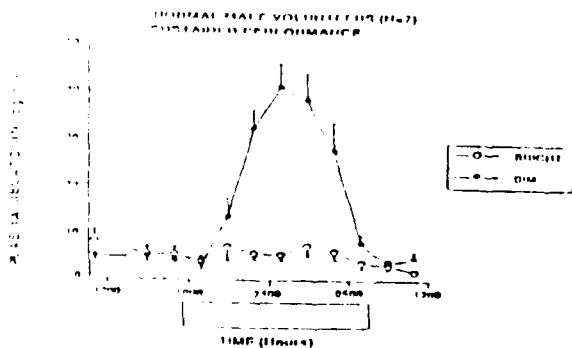
Figure 2. The suppression of normal nocturnal plasma melatonin levels was accomplished by bright light exposure. The open bar beneath the abscissa indicates the light exposure period.

Analyses of performance data indicate that bright light treatment improved response time while reducing the number of errors, particularly at the 2400 through the 0400 sample points. Table 1 shows the number of cognitive tests which were increased or decreased during bright light treatment. As shown in Table 1 the most effective time for bright light exposure to affect the cognitive tests occurred at midnight, 0200 and 0400 hrs. The effectiveness of the bright light exposure on cognitive ability did not extend beyond 0400 and may be detrimental when dim illumination is reinstated after 0600 as indicated in Table 1.

Table 1. The number of cognitive test results either increased or decreased by the application of bright lights at sequential times. A total of 10 performance tests were given at each time. The individual tests are identified (parentheses) at each time point. If response time or accuracy or if both were affected are indicated by a - or + or ±, respectively.

TIME	# OF TESTS INCREASED	# OF TESTS DECREASED
Light on		
1800	1 (CRT+)	0
2000	1 (RP+)	0
2200	1 (SAS-)	0
2400	4 (SAS- N+ W+ FD±)	0
0200	2 (SAS- N+)	0
0400	2 (SAS- N+)	0
0600	0	1 (FD±)
Light off		
0800	0	3 (FD± N+ W+)
1000	1 (SAS-)	1 (FD±)

Seven of the tests (CRT, RP, SAS, N, W, FD and MT) were sensitive to the effects of the illuminance conditions. Light exposure seemed to have beneficial effects on SAS, RP and N tasks as shown in Table 1, whereas the FD task seemed to be the most susceptible to disruption following extended exposure to bright light. Only response time performance variables were improved for the SAS test throughout the test session while the FD and W tasks demonstrated alterations in response time and accuracy variables at the times indicated. Only accuracy variables were susceptible on the N, CRT and the RP tasks. All of these results represent light x time awake interaction effects (p < .05). The bright light condition improved an accuracy variable (number of errors) on the MT as a main effect across all time points.
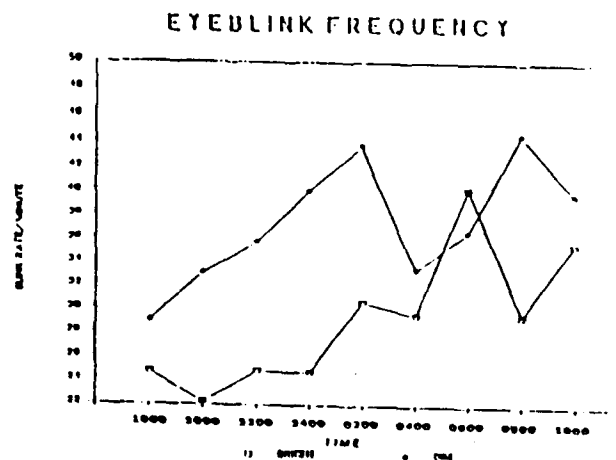
EYEBLINK FREQUENCY

Figure 3. The increase in blink frequency per minute is shown during dim light (1800 - 0600 hrs) compared to the bright light exposure.

The results shown in Figure 3 demonstrates that light treatment was associated with significant differences in eyeblink rate as determined by the EOG. An overall main effect of light on eyeblink frequency was found (p < .05) but no interaction of light condition by time was found. However, the EOG differences did not parallel the time course of the melatonin or performance variables sensitive to bright light exposure.

There was no effect on subjective mood as a result of bright light exposure. However, as the duration of the sustained performance task increased 3 mood dimensions were affected as shown in Fig. 4. Subjective impressions of confusion, fatigue and vigor as shown in Fig 4a, 4b and 4c, respectively were affected during the later trials (time) when compared to the earlier trials, independant of light condition. Accordingly, the bright and dim light groups were averaged together in Fig. 4 for each mood state and graphed across hours awake. There was no effect on subjec-

tive anger, tension or depression as a result of extended hours awake, as shown in Fig. 4d, 4e and 4f, respectively.
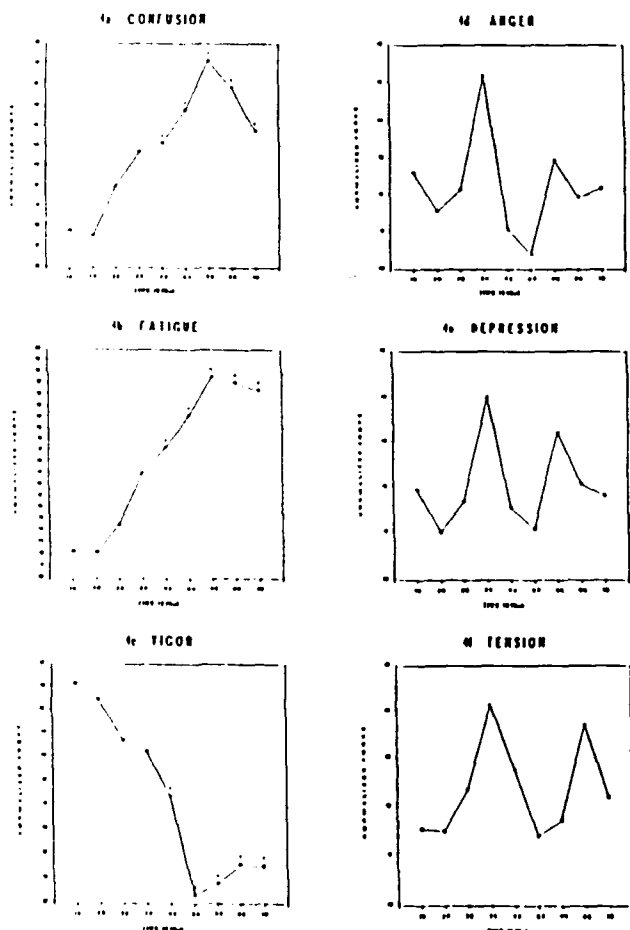

Figure 4. The effect of sustained performance on mood. No effects were found between light exposure conditions. Early trials were significantly different from later trials (p < .05) as indicated by an *. Bright and dim light groups were combined due to an absence of a light effect.

DISCUSSION

Exposure to bright light produced effects on oral temperature, melatonin levels and eye blink frequency. Although not sensitive to light condition, specific subjective mood states were responsive to the sustained performance test battery and to sleep deprivation. The times during which bright light exposure improved cognitive performance was similar to the time in which oral temperature was elevated and melatonin was suppressed. The levels of illumination used (3000 lux) were completely effective in suppressing melatonin to daytime levels. Although not excessive, 3000 lux seems to be more than adequate to control the normal nocturnal surge of melatonin.

Bright light exposure may improve performance otherwise susceptible to fatigue. However, it appears that there is no duration of the light effect beyond the exposure period. In fact, since performance begins to degrade somewhat after 10 hours of bright light exposure, the effectiveness of the lights in reducing fatigue degraded performance may have been exceeded. The absence of an interaction between light exposure and mood suggests that bright light did not improve mood state or make the the subjects feel less tired or more vigorous. Although effects on physiological state and cognitive performance were found, subjective mood was more sensitive to the duration of the sleep deprivation inherent in the 30 hour sustained performance test.

CONCLUSIONS

The protocol used may present the opportunity to evaluate adaptation problems, such as determining the optimal conditions for pre-shifting astronauts in earth bound labs. These and other problems associated with cumulative fatigue and shiftwork in the unique habitats and working conditions required in space could be studied with much greater facility in the absence of microgravity and the best solutions could then be applied to space operations. Also, the results may have implications for lighting conditions on board space flights, particularly for shift workers required to work during their subjective nights. Accuracy and response time might be improved by increased light intensity.

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Dose-dependent effects of UV-A on visual evoked potentials in humans

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Introduction

International CIE standards define the visible spectrum as wavelengths of electromagnetic radiation between 380 nm and 780 nm (1). There are, however, data demonstrating that the spectrum of radiation visible to the human eye actually extends further into the near-ultraviolet range. A recent study demonstrated that the visual system of young humans is responsive to ultraviolet radiation at least as low as 340 nm (2). The aim of the present study was to establish dose-response relationships between varying irradiances of monochromatic UV-A (340 nm) and visual evoked potentials (VEP) in young subjects.

Methods

Two age groups were examined: Children 6 to 10 years-of-age (N=6) and young adults 20 to 25 years-of-age (N=10). Each subject demonstrated 20/20 vision and an intact retina and passed an Ishihara color blindness test. VEP recording techniques and parameters were followed according to Brainard et al. (2). The 340 nm stimulus was administered by a lamp suspended 15 cm above the right eye and the left eye was patched. Seven different flash irradiances plus an auditory control were presented to each subject under ambient photopic conditions (550 lux).

Other investigators have noted the difficulty in precise measurement of irradiance emitted from extremely short (10 msec) xenon flashes (3). Therefore, preliminary irradiance measurements were made according to the following method: For each irradiance setting, separate measurements were made with a UV-A irradiance meter (Solar Light Co. Inc., Philadelphia, PA) at progressively increasing 10 unit intervals increasing from a frequency of 10 flashes/s to a maximum of 100/s. Irradiance values were plotted against flash frequency and fitted curves were used to estimate the irradiance reaching the subject's eye under experimental conditions.

The VEP is a gross electrical signal generated by the visual cortex in response to repetitive photic stimulation. Its waveform, peak latency, and amplitude vary according to experimental conditions (4, 5). Peak latencies (ms) were measured for the second negative peak, N_2, third positive peak, P_3, and third negative peak, N_3, as well as the amplitude (μV) between N_2 and P_3.

Results

Of the four variables measured, only P_3 latencies and N_2-P_3 amplitudes demonstrated irradiance-dependent changes. Consistent with the literature (6), N_2 and N_3 peak latencies remained relatively constant, and the initial components P_1, N_1, and P_2, were neither well-defined nor consistent enough to warrant measurement.

Figure 1 illustrates a dose-dependent response between irradiance and N_2-P_3 amplitude for the younger age group: As irradiance decreases, the N_2-P_3 amplitude also decreases. Figure 2 illustrates a similar dose-dependent response between irradiance and N_2-P_3 amplitude for the older age group. A comparison drawn between these two graphs demonstrates that the younger eye is more sensitive than the older eye to the UV stimulus: At an irradiance of 0.37 $\mu W/cm^2$, all six subjects in the younger age group could detect radiation whereas only two of the ten subjects in the older age group could detect this radiation; at the two lowest irradiances, one subject in the younger age group could detect radiation whereas none of the subjects of the older age group could detect this radiation. Direct statistical comparisons for identical irradiances between the two groups will be made once additional subjects are tested in the younger age group. Although not associated with statistical significance, the P_3 data demonstrated an inverse relationship between irradiance and P_3 latency.

Conclusions

This study demonstrates two major findings: First, monochromatic near-UV radiation can elicit visual evoked potentials in a dose-dependent manner in the young human
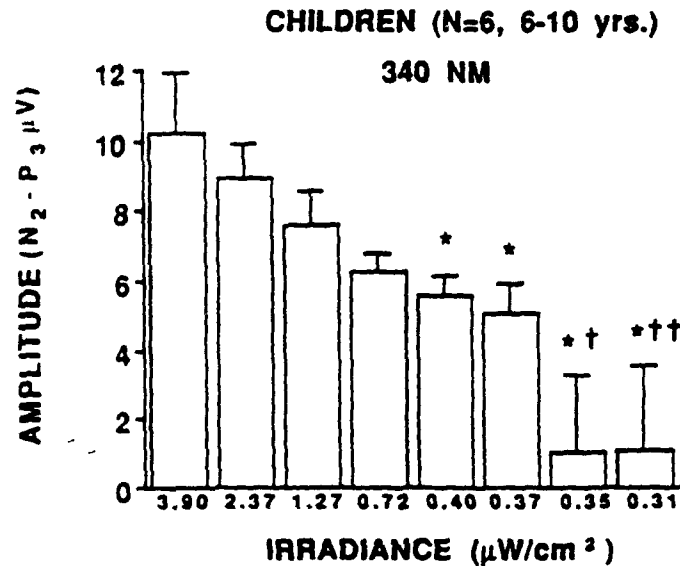
CHILDREN (N=6, 6-10 yrs.)
340 NM

Figure 1. Asterisks denote statistical significance
compared to the maximum N_2-P_3 amplitude (at the maximum
irradiance of 3.90 $\mu W/cm^2$) of at-least p<0.05; daggers
indicate that one·of the six subjects detected radiation at
the two lowest irradiances. Values were analyzed by ANOVA,
the level of statistical significanct difference was
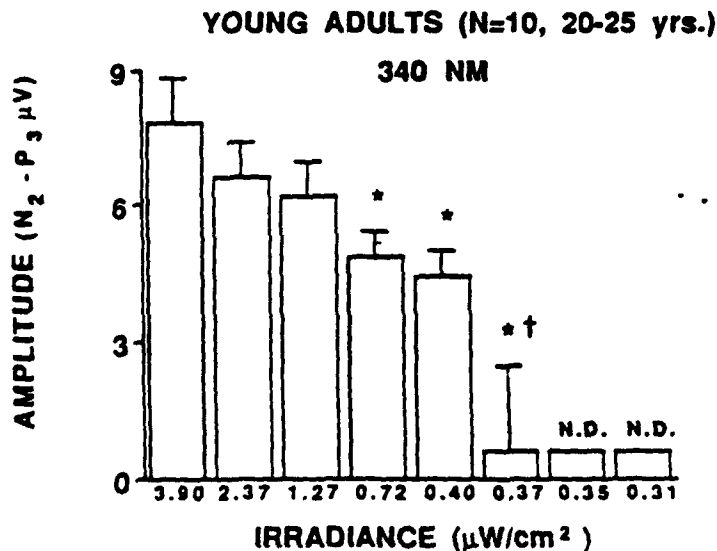determined by the Student Newman Keuls multiple range test.

YOUNG ADULTS (N=10, 20-25 yrs.)
340 NM

Figure 2. Asterisks denote statistical significance
compared to the maximum N_2-P_3 amplitude of at least p<0.05;
the dagger indicates that only one of the ten subjects was
able to detect radiation at this irradiance. N.D. = not
detected. Values were analyzed by ANOVA, the level of
statistical significanct difference was determined by the
Student Newman Keuls multiple range test.

eye. Second, this response is age-dependent: The child eye
is more sensitive than the young adult eye, as measured by
VEPs.

As demonstrated by the pioneering work of Lerman (7) and the
more recent work of Barker et al. (8), the human crystalline
lens transmits more light as one ascends from UV to infra-
red wavelengths, and the absorbance-increasing effects of
age are most prominent for near-UVR (ultraviolet radiation)
and short wavelength visible light. These events are
intimately associated with the biochemical changes occurring
within the lens concomitant with advancing age, accounting
for the increasing deposition of lenticular pigment (7).
Thus, these lenticular changes may account for the age-
related differences in UV vision existing between the two
age groups in this study.

Furthermore, because the human visual pigments demonstrate
absorption peaks within the UV range, UV-A might be expected
to elicit visual responses in human subjects. Although the
literature contains studies which describe UV vision in
humans (2, 9, 10, 11), they are based largely on
psychophysical methods of measurement. The results of the
present study objectively quantify the dose-dependent visual
response, utilizing VEP, to a wavelength of UV-A (340 nm)
radiation in children and young adults.

It is possible that secondary lenticular fluorescence, a
well-documented phenomenon elicited by incident UVR (7), may
in fact constitute the entire spectrum of radiation reaching
the retina upon fixation of a UV source by the subject.
Such fluorescence exits the lens without regard to
direction, producing a "pale bluish white" intra-ocular
"veiling glare," clouding normal vision (10, 11). This,
then, would all but preclude producing a well-focused image
on the retina. In the present study, for all but the lowest

irradiances, all subjects were able to clearly descriminate the shape of the filaments suspended within the flashlamp during stimulation. Therefore, if secondary lenticular fluorescence accounted for all the energy reaching the retina during stimulation, the subjects would not have been able to focus the image. Tan provides an elegant argument against such fluorescence-based UV vision (11).

Finally, what is the utility of perceiving UVR? As Wald first described, short wavelength radiation presents the retina with an image considerably blurred by chromatic aberration (12). Furthermore, UVR, chronic or acute, can also have deleterious effects upon the eye (13). Thus, elimination of this visually unproductive energy, e.g., by an opacifying lens, would seem advantageous. In several rodent species, however, UV-A, and even some UV-B, is transmitted through the lenses, and participates in the regulation of circadian and neuroendocrine systems (14-16). Further work is required to determine if detection of UVR by the young human eye serves some purpose other than simply vision.

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