0021-972X/01/$03.00/0
The Journal of Clinical Endocrinology & Metabolism

Vol. 86, No. 1
Printed in U.S.A.

Transition from Dim to Bright Light in the Morning Induces an Immediate Elevation of Cortisol Levels*

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ABSTRACT

The only well documented effect of light exposure on endocrine function is the suppression of nocturnal melatonin. Bright light exposure has behavioral effects, including the alleviation of sleepiness during nocturnal sleep deprivation. The present study examines the effects of bright light on the profiles of hormones known to be affected by sleep deprivation (TSH) or involved in behavioral activation (cortisol). Eight healthy men participated each in three studies involving 36 h of continuous wakefulness. In one study, the subjects were exposed to constant dim light (baseline). In the two other studies, dim light exposure was interrupted by a 3-h period of bright light exposure either from 0500–0800 h (early morning study) or from 1300–1600 h (afternoon study). Blood samples were obtained every 15 min for 24 h to determine melatonin, cortisol, and TSH concentrations. Alertness was estimated by the number of lapses on two computerized vigilance-sensitive performance tasks. The early morning transition from dim to bright light suppressed melatonin secretion, induced an immediate, greater than 50% elevation of cortisol levels, and limited the deterioration of alertness normally associated with overnight sleep deprivation. No effect was detected on TSH profiles. Afternoon exposure to bright light did not have any effect on either hormonal or behavioral parameters. The data unambiguously demonstrate an effect of light on the corticotropic axis that is dependent on time of day. (*J Clin Endocrinol Metab* **86:** 151–157, 2001)

IN HUMANS, AS in other species, the light-dark cycle is a powerful synchronizer of circadian rhythms. In particular, large shifts of hormonal profiles, including those of cortisol, melatonin, and TSH, have been observed after appropriately timed exposure to light and dark (1–5). Other than the role of light for the synchronization of 24-h hormonal rhythms, the only well documented endocrine effect of light is the suppression of nocturnal melatonin secretion that occurs within minutes of exposure to bright light (6). Conversely, the duration of nocturnal melatonin secretion is dependent on the length of the dark period (7, 8). Two recent studies, however, have suggested that hormones other than melatonin may also be affected by ambient light intensity. In a laboratory study of adaptation to simulated jet lag (9), the dark-light transition at the end of the shifted sleep period was consistently followed by a sharp rise of plasma TSH levels. The possible roles of postural changes, social interactions, and transitions from sleep to wake could not be distinguished from a putative effect of the dark-light transition *per se*. In another study in which subjects collected their own saliva while at bed rest at home (10), exposure to bright light, compared with continuous darkness, was reported to elevate saliva cortisol levels in the hour following morning awakening. It is not known whether this effect of light on cortisol concentrations can occur in the absence of sleep-wake transition.

There is evidence to indicate that exposure to bright light, compared with dim light, has general central nervous system-activating effects. A number of studies have shown that increasing light intensity reduces subjective sleepiness and limits decrements in cognitive performance, particularly during overnight sleep deprivation (11–14). Bright light exposure has, therefore, been proposed as a strategy to promote alertness in nightworkers (15–17). The time course of subjective sleepiness and/or alertness during prolonged wakefulness has been clearly defined in a number of well controlled studies (18–20). Increased sleepiness becomes apparent after 14–16 h of continuous wakefulness, *i.e.* usually during the late evening hours, at a time when the concentrations of both melatonin and TSH are increasing. In the absence of sleep, sleepiness peaks in the early morning, around the usual wake-up time, when cortisol concentrations are maximal. Sleepiness is then partly alleviated despite the increased length of wakefulness. This improvement in alertness coincides with a decline in TSH and melatonin concentrations toward lower daytime values (20).

It has been suggested that the "alerting" effects of bright light during overnight sleep deprivation may be partly exerted via the suppression of the nocturnal secretion of melatonin, a hormone with putative hypnotic properties (12). The involvement of other hormones in nocturnal decrements of alertness and their attenuation by bright light, however, cannot be excluded. It is conceivable that the alerting effects

Received March 2, 2000. Revision received July 13, 2000. Rerevision received September 6, 2000. Accepted September 13, 2000.

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* This work was supported in part by Grant DK-41814 from the NIH, Grant F49620–94-1-0203 from the U.S. Air Force Office of Scientific Research, the Mind-Body Network of the MacArthur Foundation (Chicago, IL), and the Belgian Fonds de la Recherche Scientifique Médicale. The University of Chicago Clinical Research Center is supported by NIH Grant RR-00055.

of bright light involve a stimulation of the hypothalamo-pituitary-adrenal (HPA) axis, consistent with the involvement of this axis in behavioral activation. It is also conceivable that the pronounced increase in TSH levels during overnight sleep deprivation (4, 21) plays a role in subjective fatigue and that alleviation of sleepiness by bright light exposure might be associated with changes in TSH levels.

The present study was designed to determine whether exposure to bright light, compared with dim light, has alerting effects in subjects kept continuously awake for 36 h, and whether these activating effects are related to concomitant changes in melatonin, cortisol, and TSH secretion. The experimental conditions allowed for the examination of the impact of changes in light intensity *per se*,in the absence of sleep-wake transitions and changes in activity levels, posture, and caloric intake. The subjects were exposed to bright light on two separate occasions, once in the early morning, after more than 20 h of wakefulness, when sleepiness is maximum, and once in the afternoon, after approximately 30 h of wakefulness, when a secondary peak of sleepiness consistent with the usual timing of the "postlunch dip" has been hypothesized (22).

Subjects and Methods

Subjects

Eight healthy normal male subjects (24 ± 1 yr old; body mass index, 24.1 ± 1.4 kg/m^2) participated in this study. None of the subjects had a personal history of psychiatric illness, endocrine illness, or sleep disorder. Positive criteria for selection included regular life habits with a habitual total sleep time of approximately 8 h. Shift workers and subjects having experienced a transmeridian flight less than 6 weeks before the beginning of the study were excluded.

Experimental protocol

The protocol, shown in Fig. 1, was approved by the institutional review board of the University of Chicago, and the volunteers gave written informed consent.

Each subject participated in three studies performed at approximately 2-week intervals in random order. During the baseline study, the subjects were exposed to dim light throughout the entire study. During the early morning study, continuous exposure to dim light was interrupted by exposure to bright light from 0500–0800 h. During the afternoon study, continuous exposure to dim light was interrupted by exposure to bright light from 1300–1600 h. All other aspects of the protocol were identical in the three studies. The timings of bright light exposure were selected based on the known properties of the temporal profiles of human sleep propensity and circulating melatonin levels. Early morning exposure was expected to correspond to maximum sleep propensity and high plasma melatonin levels. Afternoon bright light exposure was expected to correspond to a reported midafternoon peak of sleep propensity and to low levels of plasma melatonin (20, 22).

For 7 days before each study, the volunteers were asked to comply with a standardized schedule of sleep in total darkness: going to bed between 2300–2400 h and getting up between 0700–0800 h. Continuous recordings of wrist activity (Gähwiler Electronics, Hombrechtikon, Switzerland; or Minilogger, Minimitter Co., Inc., Sunriver, OR) were used to verify compliance.

For each study, the volunteers were admitted to the Clinical Research Center of the University of Chicago around 0830 h and received breakfast. Starting at 1000 h, they were maintained on a regimen of bedrest with enforced wakefulness in dim indoor light (<150 lux). The subjects completed at hourly intervals a visual analog scale for mood and vigor (23). Scores recorded during usual waking hours on the summary scale "overall, how do you feel?" (0 = very bad, 10 = very good) averaged 7.2 ± 1.8 in the baseline study, 7.2 ± 1.7 in the early morning study, and 7.7 ± 1.2 in the afternoon study. These scores are in the normal range for healthy nondepressed subjects. Heart rate was recorded via a Mini-Logger (Mini-Mitter Co., Inc.) throughout the study period. Two catheters were inserted, one for glucose infusion and one for blood sampling. At noon, the subjects received lunch, which constituted their last meal until the end of the study, *i.e.* until 1800 h the next day. Starting at 1400 h, caloric intake was exclusively in the form of a glucose infusion at a constant rate of 5 g/kg·24 h. At 1800 h, blood sampling at 15-min intervals for 24 h was initiated. The iv line was kept patent with a slow drip of heparinized saline.

The subjects had access to external time cues (wristwatch, radio and television programs, social contacts). Water *ad libitum* and a maximum of three diet decaffeinated sodas per day were allowed. At the end of the study, *i.e.* at 1800 h, the glucose infusion was tapered, dinner was served, and the subjects were discharged.

Procedures for light exposure

Mobile panels of mounted fluorescent tubes, providing a light intensity of 16,000 lux at a distance of 0.30 m, were placed in front of the subjects at about a distance of 1.5 m. In addition, light boxes, providing a light intensity of 14,000 lux at a distance of 0.30 m, were placed on each side of the bed. Illumination levels at the subject's eye were regularly checked using a digital light meter (Research Products International Corp., Mount Prospect, IL). Each 3-h period of exposure to bright light included successively 15 min of illumination at 2000–2500 lux, 45 min of illumination at 3000–4000 lux, 1 h of illumination at 4500 lux, 45 min of illumination at 3000–4000 lux, and 15 min of illumination at 2000–2500 lux.

Hormonal assays

Plasma melatonin levels were measured with a double antibody RIA using commercially available reagents (Stockgrand, Guilford, Surrey, UK) as previously described (24). The lower limit of sensitivity of the assay was 11 pmol/L. The intraassay coefficient of variation averaged

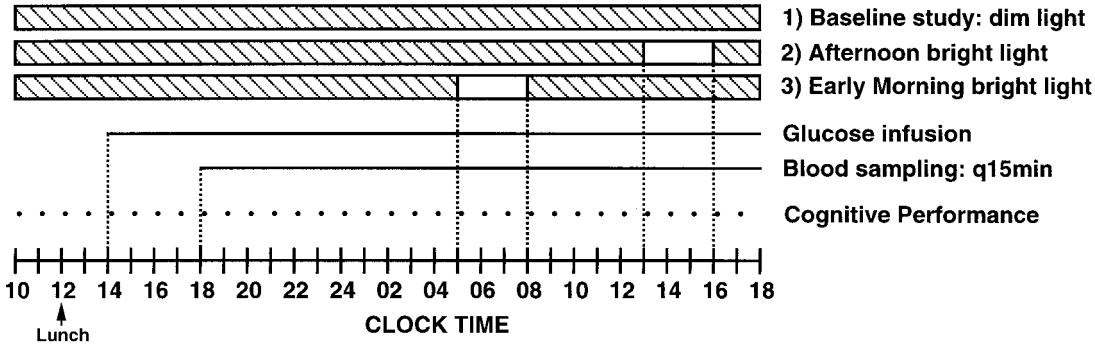

FIG. 1. The protocol consisted of three studies: a baseline study with dim light throughout, an afternoon study with bright light exposure between 1300–1600 h, and an early morning study with bright light exposure between 0500–0800 h. The *shaded bars* indicate dim light exposure, whereas the *white bars* indicate periods of bright light exposure.

17.5% for values less than 43 pmol/L and 8.6% for values greater than 43 pmol/L.

Plasma cortisol levels were measured by a chemiluminescent enzyme immunometric assay (Immulite, Diagnostic Products Corporation, Los Angeles, CA) with a lower limit of sensitivity of 28 nmol/L. The intraassay coefficient of variation averaged 6%.

Plasma TSH levels were measured by a chemiluminescent enzyme immunometric assay (Immulite Third Generation TSH, Diagnostic Products Corp, Los Angeles, CA). The sensitivity of the assay was 0.002 μU/mL. The intraassay coefficient of variation averaged 2% in the physiological range. For all hormonal determinations, samples from the same subject were measured in the same assay run.

Estimation of vigilance

Two cognitive performance tasks, a perceptual cueing task and a vigilance task that are part of the Harvard Cognitive Performance Battery (Department of Psychology, Harvard University, Boston, MA), were administered hourly on portable computers. Four versions of each task were created to avoid learning effects. Each task took approximately 2 min to complete.

The perceptual cueing task measures both the strength of a subject's attention and the ease with which that attention can be shifted. This task included 40 trials for which the subject has to press the space bar as fast as possible in response to each trial. The vigilance task measures the ability of a subject to sustain attention in the absence of salient signals. This task contains 48 trials. For both tasks, the reaction time is measured for each trial.

For each subject and for each task, lapses were defined as reaction times that exceeded the 99th percentile of the distribution of reaction times measured in each study during the normal waking period, *i.e.* the time interval 1000–2300 h. For each individual and for each study, the total number of lapses on each task was determined, and an objective hourly measure of sleepiness was obtained by adding the number of lapses on the two tasks.

Statistical tests

All group values were expressed as the mean ± SEM. All statistical calculations were performed using nonparametric tests (Friedman procedure for three repeated measures and Wilcoxon test for two repeated measures) with the StatView SE$^+$ software (Abacus Concepts, Inc., Berkeley, CA) for Macintosh computers. Correlations were calculated using the Spearman rank coefficient of correlation (r_S).

Results

Figure 2 shows the TSH, melatonin, and cortisol profiles for the three studies. Under baseline conditions, the profiles of the three hormones conformed with previous observations in normal subjects undergoing 1 night of total sleep deprivation (20).

Effects of bright light exposure on hormonal profiles

TSH profiles (*left panels* of Fig. 2) were similar in the three study conditions, and in particular, there were no significant effects of exposure to bright light either in the morning or in the afternoon.

As expected, early morning bright light exposure resulted in an immediate inhibition of melatonin secretion (*lower mid-*

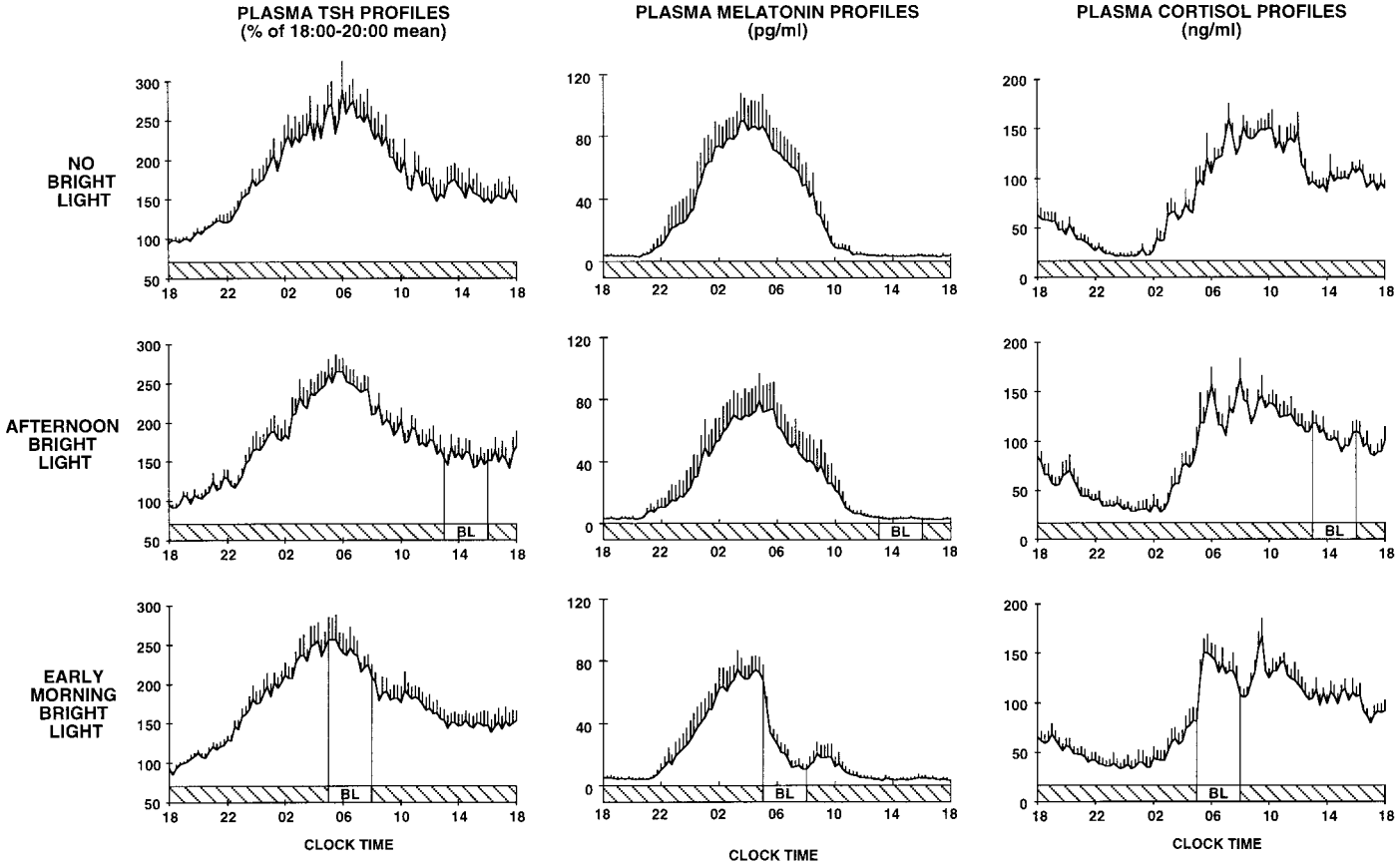

FIG. 2. Transverse means (+SEM) across the eight subjects of plasma TSH, plasma melatonin, and plasma cortisol levels in the three studies. The *shaded bars* indicate dim light exposure, whereas the *white bars* indicate periods of bright light exposure (BL). Because of the interindividual variability, TSH data were expressed for each subject and each study relative to the 1800–2000 h mean.

dle panel of Fig. 2). Melatonin levels averaged 292 ± 43 pmol/L in the sample preceding the increase in light intensity and decreased to 215 ± 30 pmol/L within 15 min and to 151 ± 17 pmol/L within 30 min of turning on the light banks ($P < 0.005$). After this initial rapid inhibition, melatonin levels continued to decrease at a slower rate during the next 2 h. Melatonin levels from 0515 until 0800 h, *i.e.* during the period of exposure to bright light in the early morning study, averaged 95 ± 17 pmol/L in the early morning study compared with 280 ± 56 pmol/L in the baseline study and 245 ± 60 pmol/L in the afternoon study ($P < 0.02$). For all three study conditions, consistent with the known characteristics of the circadian rhythm of pineal secretion, melatonin levels were low in the afternoon and were not affected by bright light exposure at this time of day (*middle panels* of Fig. 2). Melatonin levels from 1315 until 1600 h, *i.e.* during the period of exposure to bright light in the afternoon study, averaged 13 ± 4 pmol/L in the early morning study, compared with 17 ± 4 pmol/L in the baseline study and 17 ± 4 pmol/L in the early morning study.

A robust effect of bright light exposure was observed in the cortisol profiles in the early morning, but not in the afternoon (*right panels* of Fig. 2). The time course of changes in cortisol levels associated with early morning changes in light intensity compared with constant dim light is further illustrated in the *left panels* of Fig. 3. Within 15 min of the transition from dim light to bright light, a robust elevation of plasma cortisol was detected in all individual profiles. On the average, cortisol levels increased from 223 ± 33 nmol/L at 0500 h, *i.e.* just before the increase in light intensity, to 348 ± 47 nmol/L at 0515 h ($P < 0.02$). The elevation in cortisol levels from 0500–0515 h averaged 121 ± 19 nmol/L and was larger than increases occurring at the same clock time in the baseline (17 ± 19 nmol/L; $P < 0.01$) or the afternoon studies (66 ± 41 nmol/L; $P = 0.12$). The fact that the difference between the early morning and the afternoon studies failed to reach significance reflects the presence of a large afternoon cortisol elevation (342 nmol/L) in a single subject. If this subject is excluded from that comparison (n = 7 instead of n = 8), the elevation of cortisol levels from 0500–0515 h averaged 113 ± 19 nmol/L in the early morning study and was larger than increases occurring in the same clock time in the baseline (28 ± 19 nmol/L; $P < 0.02$) or the afternoon (25 ± 14 nmol/L; $P < 0.02$) studies. After this initial rise associated with the transition from dim to bright light, cortisol levels decreased slowly throughout the period of bright light exposure (Fig. 3) and averaged 295 ± 19 nmol/L during the time interval 0800–0830 h, following the end of bright light exposure. A consistent rebound of cortisol concentrations followed, with levels reaching 403 ± 33 nmol/L ($P < 0.02$) during the time interval 0900–0945 h. Interindividual synchronization of short-term increases and decreases in cortisol levels did not occur at the same clock times in either the baseline study or the afternoon study. In the afternoon study, changes in light intensity had no detectable effect on cortisol profiles (Fig. 2).

The rapid elevations in cortisol levels after early morning transition from dim to bright light did not appear related to an acute stress effect, as they were not accompanied by increases in heart rate (*right panels* of Fig. 3).

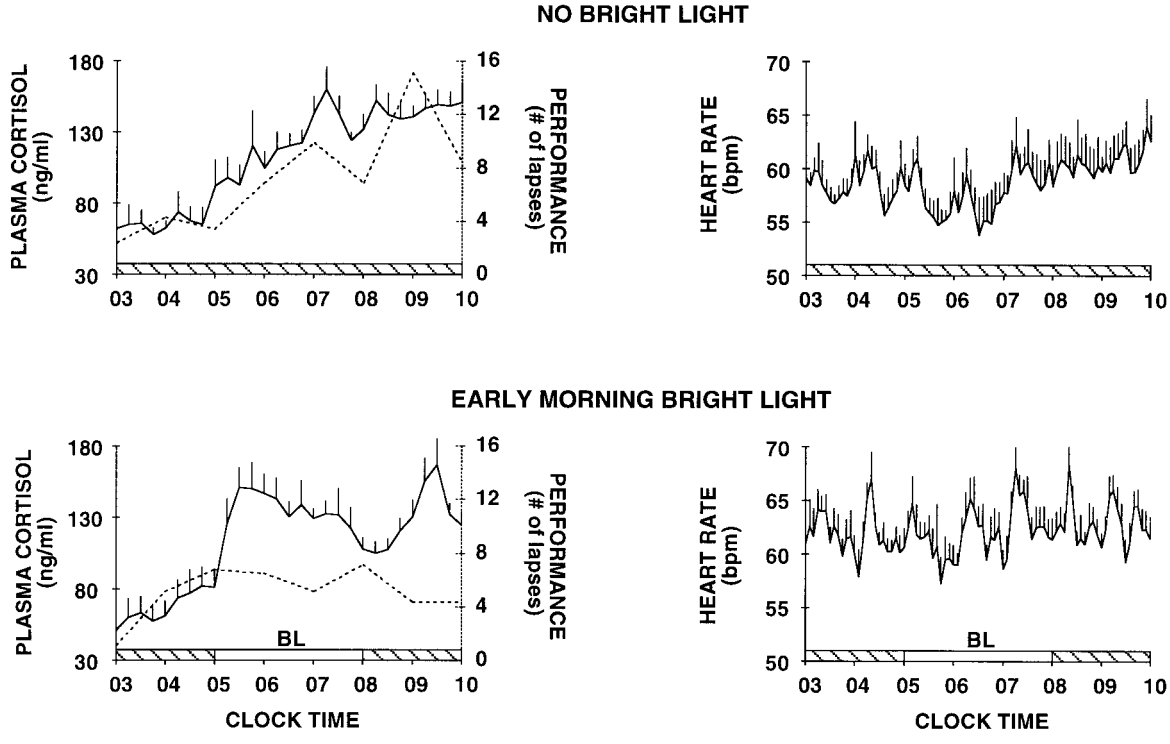

FIG. 3. Transverse means (+SEM) across the eight subjects of plasma cortisol and heart rate between 0300–1000 h in the baseline and early morning studies. *Dashed lines* on the *left panels* represent the mean of the number of lapses on performance tasks. The *shaded bars* indicate dim light exposure, whereas the *white bars* indicate periods of bright light exposure (BL).

Effects of bright light exposure on cognitive performance

Figure 4 shows the mean profiles of the number of lapses on performance tasks for the three studies. Performance showed no major changes from morning until the early part of the usual sleep period. Indeed, from 1000 until 0200 h, the number of lapses remained low at 1.0 ± 0.1 in all three studies. The number of lapses then started to increase, indicating a deterioration of performance.

Differences between the three studies in the rate of increase in the number of lapses became apparent over the period 0500–1000 h, *i.e.* from the time of the transition from dim to bright light in the early morning study until 2 h after the end of bright light exposure. Indeed, over this time period, the number of lapses increased at a similar rate in the two studies with constant dim light (baseline study, 1.3 ± 0.5 lapses/h; afternoon study, 1.2 ± 0.5 lapses/h). In contrast, in the study with early morning bright light exposure, the number of lapses did not increase over the same time period (−0.5 ± 0.2 lapses/h; $P = 0.03$). This impact of morning bright light on the rate of performance deterioration was maintained throughout the period of exposure, and the number of lapses did not increase until 2 h after return to dim light conditions. Thus, although in the baseline and afternoon studies, peak sleepiness occurred at 0845 ± 29 and 0822 ± 69 min, respectively, peak sleepiness was delayed until 1131 ± 80 min in the study with early morning bright light (Fig. 4; $P < 0.05$). The level of peak sleepiness, as estimated by the maximum number of lapses, did not differ significantly across the three study conditions (16.1 ± 2.2 lapses in the baseline study, 18.2 ± 3.0 in the afternoon study, and 14.8 ± 3.5 in the early morning study).

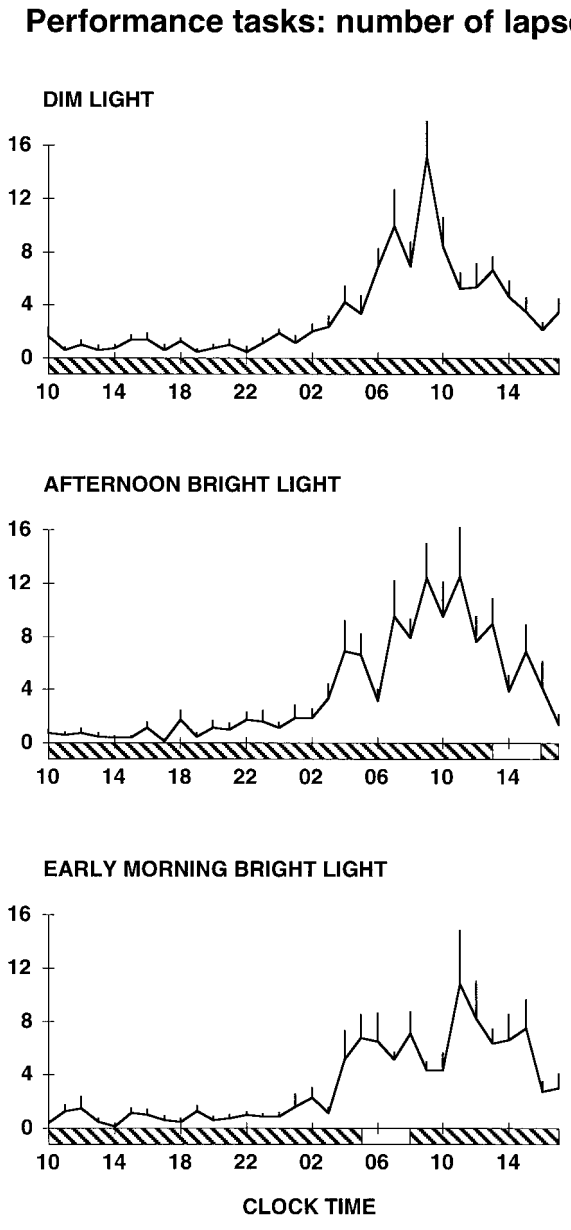

FIG. 4. Transverse means (+SEM) across the eight subjects of the number of lapses on the perceptual cueing task and the vigilance task in the three studies. The *shaded bars* indicate dim light exposure, whereas the *white bars* indicate periods of bright light exposure.

In all three studies, performance steadily improved in the late morning and afternoon despite the persistence of total sleep deprivation. There was no immediate effect of afternoon exposure to bright light on cognitive performance.

Correlations of hormonal and performance changes after early morning bright light

During the first 15 min of bright light exposure, the sharp increases in cortisol levels were not significantly correlated with the concomitant decreases in melatonin levels ($r_S = -0.47$; $P = 0.22$). However, the decreases in melatonin after 30 min of bright light were significantly correlated with the increase in cortisol levels observed during the first 15 min ($r_S = -0.80$; $P = 0.03$).

We also sought to determine whether alleviation of performance deterioration during bright light exposure (as estimated by the slope of the number of lapses) was correlated with the magnitude of melatonin suppression or/and the magnitude of the cortisol elevation. There were no significant correlations between performance changes and initial melatonin decreases. In contrast, a trend for a negative correlation between the slope of the number of lapses and the magnitude of the acute cortisol response to light was apparent ($r_S = -0.62$; $P = 0.10$). Thus, the subjects who maintained the best performance levels (*i.e.* had the lowest rate of increase in number of lapses) during the period of bright light exposure were those who had the largest acute cortisol responses after the transition from dim to bright light. The *left panels* of Fig. 3 show the simultaneous profiles of plasma cortisol and number of performance lapses for the baseline study and the study with early morning bright light.

Discussion

Under well controlled conditions of constant recumbent posture, constant wakefulness, constant caloric intake, and constant activity levels, the present study demonstrated a previously unrecognized effect of changes in ambient light intensity on cortisol levels that is dependent on time of day. The transition from dim light to bright light, achieved by a stepwise increase from less than 150 lux (low indoor light intensity) to 4500 lux (outdoor light intensity on a cloudy

day) to avoid startling effects induced a rapid and robust 110–140 nmol/L increase in plasma cortisol levels in the early morning, but not in the afternoon. This cortisol elevation occurred in the absence of identifiable stimuli that could have evoked a stress response and was not associated with significant changes in heart rate. Early morning exposure to bright light limited the deterioration of alertness normally associated with overnight sleep deprivation and, as expected, inhibited melatonin secretion. In contrast, increased light intensity in the afternoon had no effect on melatonin levels, cortisol levels, or number of performance lapses.

During the past decade, a number of studies have indicated that morning awakening is consistently followed by a short-term increase in cortisol levels (25, 26). Recently, Scheer *et al.* showed that this morning postawakening cortisol elevation, which occurs even in continuous darkness, can be enhanced by increasing light intensity. Available evidence from studies in night workers and from analyses of awakenings interrupting sleep indicates that a pulse in cortisol secretion consistently follows the sleep-wake transition regardless of time of day (27, 28). In contrast, the present data and limited evidence from a recent study (10) indicate that the impact of increased light intensity on cortisol levels is dependent on time of day. The present study further demonstrates that the stimulatory effect of early morning bright light on cortisol levels may occur in the absence of a sleep-wake transition. Thus, under normal conditions of nocturnal bedtimes, both sleep-wake and dark-light transitions contribute to amplify the morning acrophase of the circadian rhythm of cortisol secretion.

In mammalian species, the 24-h rhythms of cortisol and melatonin secretions are dependent on an endogenous circadian periodicity generated in the suprachiasmatic nuclei (SCN) of the hypothalamus. Light is the major environmental factor responsible for the synchronization of circadian rhythms. Light information is transmitted from the eyes to the SCN via a specific neuroanatomical pathway, the retinohypothalamic tract (29). Efferent projections from the SCN to CRF-containing neurons in the paraventricular nucleus are thought to be involved in the entrainment of the 24-h rhythm in HPA activity and its photic synchronization. The melatonin rhythm is regulated by the SCN through a multisynaptic projection to the pineal gland that begins with a projection from the SCN to the paraventricular nucleus. Melatonin suppression is maintained as long as light signals are transmitted from the retina to the SCN and to the pineal gland. In contrast, the present data suggest that activation of the HPA axis is an acute response to the increase in light intensity. Although the anatomical and neurochemical mechanisms by which light via the SCN suppresses melatonin production are well understood, nothing is known about the mechanisms by which light can directly affect the HPA axis. In the human, exposure to light in the early morning results in advances of circadian phase, whereas exposure to light during the afternoon does not cause detectable shifts in circadian phase (4, 30–35). The fact that the effects of light on cortisol levels and cognitive performance observed in the present study were also dependent on the timing of exposure suggests that these short-term effects of light could be mediated by the SCN. Alternatively, direct retinal projections to other areas of the hypothalamus have been evidenced (29) and could mediate the acute effect of light on cortisol levels observed in the present study (36).

After the increase in light intensity in the early morning, melatonin levels decreased sharply during the first 30 min and then continued to decline slowly, whereas cortisol levels augmented sharply and then steadily decreased. The magnitudes of the rapid cortisol and melatonin changes associated with the dim to bright light transition were negatively correlated, suggesting that common mechanisms, possibly mediated by the SCN, may have been involved in the initial, but not the sustained, effects of increased light intensity.

Our study also provides limited evidence for a relationship between improved performance and bright light-induced cortisol elevations, but not melatonin declines. Although the present analyses do not permit the exclusion of a role for melatonin suppression in the alerting effects of nocturnal bright light, they suggest that an activation of the HPA axis could also be involved, at least when exposure occurs in the early morning hours.

No effect of light exposure on TSH levels could be detected either in the early morning or in the afternoon. The fact that early morning bright light attenuated vigilance deficits in the absence of detectable effects on TSH levels suggests that the large TSH increase normally associated with nocturnal sleep deprivation does not play a major role in causing fatigue. The lack of effect of light on TSH in the present study also suggests that the sharp increases in TSH levels seen after an afternoon dark-light transition in a previous study (9) involved nonphotic factors, *e.g.* postural changes, sleep-wake transition, and social stimulation.

In conclusion, the present study demonstrates that in healthy young men, cortisol secretion can be stimulated by photic inputs in the morning, but not in the later part of the day, and suggests that the impact of light on HPA activity is mediated by the central circadian pacemaker located in the SCN. Further studies are needed to determine whether similar effects of morning light on cortisol levels occur in women and older adults.

Acknowledgments

We thank the volunteers for their participation in these demanding studies. We thank Prof. S. M. Kosslyn (Department of Psychology, Harvard University) for providing the Harvard Cognitive Performance Battery.

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