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Time-of-day-dependent effects of bright light exposure on human psychophysiology: comparison of daytime and nighttime exposure

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Rüger, Melanie, Marijke C. M. Gordijn, Domien G. M. Beersma, Bonnie de Vries, and Serge Daan. Time-of-day-dependent effects of bright light exposure on human psychophysiology: comparison of daytime and nighttime exposure. *Am J Physiol Regul Integr Comp Physiol* 290: R1413–R1420, 2006. First published December 22, 2005; doi:10.1152/ajpregu.00121.2005.—Bright light can influence human psychophysiology instantaneously by inducing endocrine (suppression of melatonin, increasing cortisol levels), other physiological changes (enhancement of core body temperature), and psychological changes (reduction of sleepiness, increase of alertness). Its broad range of action is reflected in the wide field of applications, ranging from optimizing a work environment to treating depressed patients. For optimally applying bright light and understanding its mechanism, it is crucial to know whether its effects depend on the time of day. In this paper, we report the effects of bright light given at two different times of day on psychological and physiological parameters. Twenty-four subjects participated in two experiments (*n* = 12 each). All subjects were nonsmoking, healthy young males (18–30 yr). In both experiments, subjects were exposed to either bright light (5,000 lux) or dim light <10 lux (control condition) either between 12:00 P.M. and 4:00 P.M. (*experiment A*) or between midnight and 4:00 A.M. (*experiment B*). Hourly measurements included salivary cortisol concentrations, electrocardiogram, sleepiness (Karolinska Sleepiness Scale), fatigue, and energy ratings (Visual Analog Scale). Core body temperature was measured continuously throughout the experiments. Bright light had a time-dependent effect on heart rate and core body temperature; i.e., bright light exposure at night, but not in daytime, increased heart rate and enhanced core body temperature. It had no significant effect at all on cortisol. The effect of bright light on the psychological variables was time independent, since nighttime and daytime bright light reduced sleepiness and fatigue significantly and similarly.

sleepiness; core body temperature; cortisol; heart rate

BRIGHT LIGHT IS A prominent agent influencing human psychophysiology. Besides the ability to reset or shift the biological clock (6, 25, 27, 38, 44, 50), bright light is thought to have an immediate activating effect on the central nervous system. This immediate effect has been studied mostly in the context of prolonged wakefulness to explore beneficial effects of bright light on alertness and performance, for instance in shift workers. Nighttime bright light exposure is known to reduce sleepiness (11, 13, 44), enhance alertness (3, 5, 12, 17, 39), and to improve mood and performance in healthy subjects (16, 21, 40). At the same time, it suppresses melatonin, enhances core body temperature (CBT), and increases heart rate (35, 44, 46, 48). Because the reduction of sleepiness is often accompanied by the suppression of nocturnal melatonin and/or the increase

in CBT, it is sometimes assumed that melatonin is the causal factor in this process (4, 9, 22). However, data from daytime bright light exposure studies show that bright light can reduce sleepiness even though melatonin is virtually absent and CBT is nearly constant (42, 43). We have shown that the relation between melatonin suppression and reduction of sleepiness/fatigue is weak, and therefore, melatonin suppression cannot be the sole explanation for the activating properties of bright light (45).

Few studies have focused on the effects of light on the autonomic nervous system. The results of these studies are moreover difficult to compare because they vary greatly in the amount of light used and in output variables measured. Saito et al. (46) and Scheer et al. (48) showed an increase in muscle sympathetic nerve activity and heart rate in response to bright light, and Gilbert and coworkers (22) found a reduction of the heart rate of healthy young males after the administration of exogenous melatonin (5 mg) during the afternoon. Burgess et al. (8) failed to find a clear effect of bright light on cardiac output measures such as respiratory sine arrhythmia, preejection period, and diastolic blood pressure. Tsunoda et al. (50) observed an increase in the low frequency-to-high frequency ratio of the heart rate variability after bright light exposure and after exposure to complete darkness. Besides heart rate variability, cortisol also shows a clear circadian rhythm with a peak around awakening (31). The circadian rhythm in cortisol is largely under the control of the circadian pacemaker in the suprachiasmatic nucleus (SCN; see Ref. 7). Therefore, it is to be expected that the rhythm and the concentration of cortisol will be influenced by light. Indeed Leproult et al. (33) showed that in sleep-deprived subjects, 3 h of bright light exposure (4,500 lux) in the early morning (5:00–8:00 A.M.) induced an increase in cortisol levels, whereas afternoon (1:00–4:00 P.M.) bright light exposure had no effect on cortisol. The cortisol peak after awakening is present in total darkness and can be enhanced by 1 h of 800 lux applied at habitual time of waking (47). Thorn et al. (49) showed that gradually increasing luminance levels (250 lux over 30 min) during awakening (dawn simulation) increased cortisol levels compared with the control condition, in which subjects used their regular alarm clock to wake up, without additional increasing luminance. This increase in cortisol was accompanied by a higher level of reported arousal but not of reported stress.

Although the literature suggests that some of the variance in the responses to bright light may be associated with time of day, there is no straightforward analysis of such variation in

human psychophysiological variables (14, 15, 42, 43). The fields of bright light application can range from clinical (light therapy of Seasonal Affective Disorder patients and sleep disorder patients) to work (improving work environment for shift workers) settings, and it is crucial to know to what extent immediate effects of bright light on human psychophysiology are time-of-day dependent.

For this reason, we compared two data sets of daytime and nighttime bright light exposure, 12 h out of phase with each other, in humans and their effects on sleepiness, fatigue, and energy (psychological variables) as well as CBT, cortisol, and heart rate (physiological variables). Twenty-four subjects participated in the two studies and were exposed to 4 h of 5,000 lux of bright light either between noon and 4:00 P.M. (daytime experiment) or between midnight and 4:00 A.M. (nighttime experiment).

METHODS

Subjects

Twenty-four healthy male subjects participated in the two experiments, twelve in each [daytime experiment: mean age, 23.1 (SD 1.5) yr; nighttime experiment: mean age, 21.8 (SD 1.9) yr, $P > 0.05$]. Subjects were screened using a general health questionnaire and a Morningness-Eveningness Questionnaire (MEQ; see Ref. 26). Only healthy, nonsmoking subjects with intermediate MEQ scores (i.e., scores between 31 and 69) were selected. Subjects had to be without current medication or psychiatric illness; they neither worked night shifts nor did they recently (within the last month) travel more than one time zone. They were instructed to keep a regular sleep schedule during the week before entering the study, i.e., to sleep within the interval from midnight until 8:00 A.M. Midsleep and sleep duration were calculated based on the information of the health questionnaire that subjects had to fill out during the screening procedure {midsleep: *experiment A* 3:51 h $\pm$ 45 min vs. *experiment B* 4:28 h $\pm$ 30 min, [$t(22,2) = 2.323$, $P = 0.030$]; sleep duration: *experiment A* 8:12 h $\pm$ 52 min vs. *experiment B* 8:35 h $\pm$ 40 min [$t(22,2) = 1.474$, $P =$

0.155, not significant]}. Subjects gave written informed consent and were paid for their participation. The medical ethics committee of Groningen University approved the protocol.

Time Isolation Facility

The protocol included either two stays of 1.5 days (*experiment A*: daytime bright light and dim light exposure) or three stays of 2.5 days (*experiment B*: nighttime bright light, dim light, and extraocular light exposure) each in the time isolation facility. Results from the comparison of nighttime extraocular and ocular light exposure have been reported elsewhere (43). The facility, where neither daylight nor clock information is present, can host four subjects simultaneously in separate rooms. Subjects could read or study, listen to music, watch videos, or perform other nonphysical activities. Light sources present in the isolation facility did not exceed 10 lux measured at eye level and direction of gaze at any position in the room.

Consumption of tea, coffee, chocolate, and bananas was not allowed because these substances influence serotonin concentration, which is the precursor of melatonin; furthermore, they may contaminate the saliva sample and therefore interfere with the results of the RIA used to determine the melatonin concentration (24).

Experimental Protocol

Experiment A (daytime bright light) took place from May until December 2001, and *experiment B* (nighttime bright light) took place from July until October 2000. For both experiments, the time interval between sessions ranged from 1 wk up to 3 wk. In each session, subjects were exposed to one of the two light treatments in counterbalanced order.

Both protocols consisted of the same set of measurements but differed in timings of light exposure, testing periods, and sleeping periods. The protocols are summarized in Fig. 1. In *experiment A* (daytime exposure), subjects entered the facility at 4:00 P.M. on *day 0*. Electrodes were fitted for recording EEG and ECG. The EEG results will be reported elsewhere. At the same time, the test battery was introduced and explained, and continuous measurement of rectal temperature was started. Subjects were free to read or watch videos between test batteries. During the intervals of light exposure, they
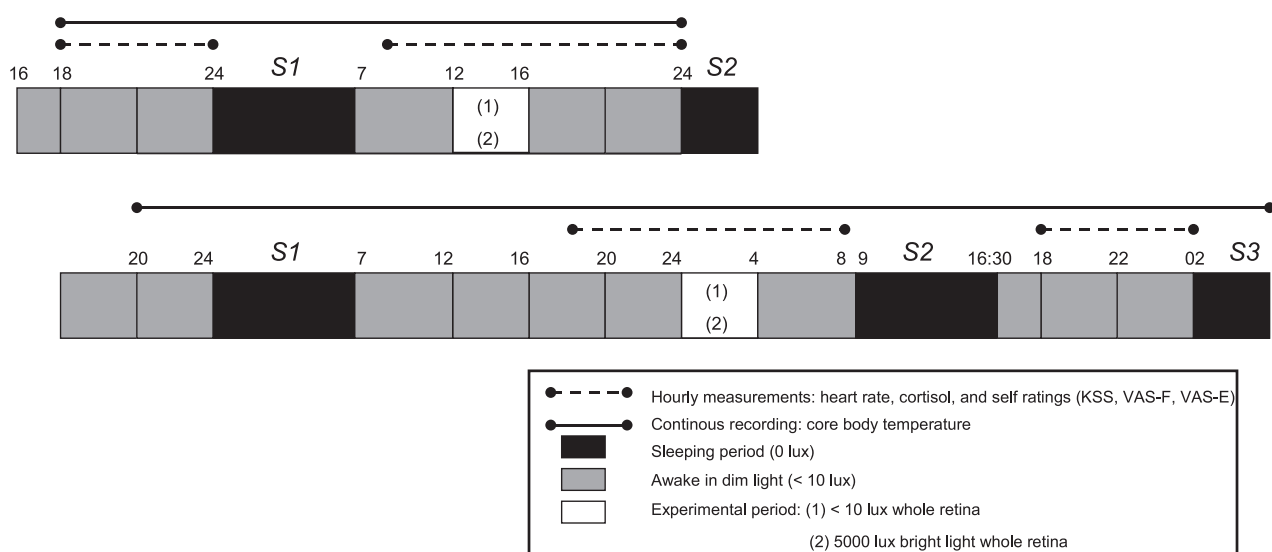
Fig. 1. Experimental design of the two experiments. *Top*: daytime bright light experiment. *Bottom*: nighttime experiment. Wake periods in dim light (<10 lux) are indicated by gray bars, sleeping periods by solid bars (*S1–S3*), and periods of light exposure or dim light control by white bars. The lengths of the last sleeping periods of each experiment (*S2* for *experiment A* and *S3* for *experiment B*) varied since they were terminated by the subjects and not by the protocol. Solid lines indicate the periods of continuous measurements, and dashed lines indicate the periods of hourly measurements. Each subject participated in both the bright light and the dim light control condition, in a crossover design. KSS, Karolinska Sleepiness Scale; VAS-F, Visual Analog Scale for fatigue; VAS-E, Visual Analog Scale for energy.

were only allowed to read but not to watch videos. At 6:00 P.M. of *day 0*, the first testing period (*testing 1*) with hourly measurements started, including the test battery, 6 min of wake-EEG (3 min eyes open followed by 3 min eyes closed) and ECG recording, and a saliva sample was taken for the determination of cortisol concentration. Fifteen minutes before each test battery (duration ~20 min), subjects had to remain seated upright in their chair without moving, since the change of position is known to influence hormonal concentrations (18). Warm meals were scheduled at the same time for all subjects, and snacks and beverages were available on request. No food or beverage consumption was allowed in the 45-min interval before the collection of a saliva sample. After each consumption, the subjects had to rinse their mouth with water to prevent contamination of the next saliva sample. At midnight, subjects went to bed, and the first sleep period (*sleep 1*) was recorded. Subjects woke at 7:00 A.M. the following day (*day 1*) and had breakfast and a shower. The second testing period (*testing 2*) started at 8:00 A.M. and lasted until midnight. During this period, subjects received either 5,000 lux of bright light or <10 lux of dim light from noon until 4:00 P.M. From midnight onward, the second sleep period was recorded (*sleep 2*), including spontaneous sleep termination, i.e., the subjects were instructed to sleep as long as they wanted and to give a sign via the intercom when they felt refreshed and wanted to get up.

Experiment B (nighttime exposure) consisted of an adaptation night (*day 0*) that was followed by 26 h of sustained wakefulness, starting at 7:00 A.M. on *day 1*. The first testing period (*testing 1*), including the previously explained measurements, started at 6:00 P.M. on *day 1* and lasted until 9:00 A.M. on *day 2*. During this period of 26 h of sustained wakefulness, the subjects were exposed to 5,000 lux of bright light or <10 lux of dim light from midnight until 4:00 A.M. (see Fig. 1). From 9:00 A.M. until 4:30 P.M. (*day 2*), the second sleep period (*sleep 2*) was recorded. At 4:30 P.M. (*day 2*), subjects were awakened again; they had breakfast and took a shower, and at 6:00 P.M. the second testing period (*testing 2*) started, which lasted until 2:00 A.M. of the next day (*day 3*). From 2:00 A.M. onward, the third and last sleep period (*sleep 3*) was recorded, the length being determined by the subject as in *experiment A*.

Light Exposure

During both experiments, light intensity was <10 lux except for the period of light exposure (daytime experiment: noon until 4:00 P.M., nighttime experiment: midnight until 4:00 A.M.) and the sleeping periods (lights off = 0 lux). In both experiments we used Bright Light boxes (Philips, Eindhoven, The Netherlands) that were placed vertically in front of the subject next to a computer screen. Subjects remained seated in front of the computer screen during the 4 h of bright light or dim light exposure and were instructed to look at the light source regularly. During the control condition (dim light exposure), the subjects also remained seated for 4 h in front of the personal computer without the lamps being turned on. Luminance of the bright light exposure was 5,000 lux at eye level, measured in the direction of gaze. Because subjects were allowed to read during the light exposure and therefore looked downward, the average light intensity to which subjects were exposed would have been lower than 5,000 lux at times. Subjects were exposed to the bright light or the dim light condition in a counterbalanced order. Wakefulness of the subjects was verified through online recording of the EEG.

Physiological Parameters

Heart rate. An ECG was obtained using disposable, single-use, pregelled electrodes (Red Dot; 3M Health Care, Borken, Germany), which were placed at the positions V_6 and the right collarbone (bipolar Wilson lead) of the subjects. The ground electrode was the same used for the EEG recordings, which was placed on the forehead of the subjects. ECG and EEG were recorded hourly for 6 min (3 min with eyes open and 3 min with eyes closed) during the testing periods.

Heart rate was calculated as beats per minute, dividing the total amount of heart beats of each of the 3-min periods by three. There was no significant difference between the data from the two 3-min periods (eyes closed and eyes open); therefore, we present the combined data.

Cortisol. Cortisol concentrations were measured in saliva. Subjects gave a saliva sample before each test battery, i.e., one time per hour. Saliva was collected using Sarstedt Salivettes with a polyester swab. Samples were centrifuged immediately and stored at −20°C. Cortisol concentration was determined using an RIA (Spectria, ^{125}I-labeled cortisol, Coated Tube Radioimmunoassay; Orion Diagnostics, Espoo, Finland). The mean value of duplicate samples was taken for the cortisol concentration. The limit of detection for the cortisol RIA was 0.8 nmol/l with an intra-assay variation of 7.5% at a low concentration (4.1 nmol/l) and 4.0% (16.5 nmol/l) at a high concentration. The interassay variation was 8.6% at a low concentration (4.1 nmol/l) and 4.9% at a high concentration (16.6 nmol/l).

CBT. CBT was recorded by a rectal probe. The thermometer was connected to a portable registration system (JOBLOG; Ref. 5a) that records temperature at 1-min intervals with a resolution of 0.05°C. Data on CBT were occasionally missing because of sanitary requirements or technical failure. Missing data of <90 min were reconstructed by linear interpolation. Missing data of >90 min were recorded as missing. Only subjects with complete data sets in both conditions were included in the temperature analysis. This resulted in a sample size of 10 subjects for the daytime experiment and 7 subjects for the nighttime experiment.

Test Battery: Psychological Parameters

Sleepiness, fatigue, and energy. The subjective feelings of sleepiness, fatigue, and energy were assessed by the use of three questionnaires [the Karolinska Sleepiness Scale (KSS; see Ref. 2) and the Visual Analog Scale for fatigue (VAS-F) and energy (VAS-E; see Ref. 32)]. Every hour, subjects completed the questionnaires electronically on a test personal computer from which the clock function was disabled.

Statistical Analysis

The activating effects of bright light were tested using repeated-measures ANOVAs for the within-subjects factors condition (dim vs. bright light), exposure (before vs. during the light exposure), and time (daytime experiment: 9:00, 10:00, and 11:00 A.M. vs. 1:00, 2:00, and 3:00 P.M.; nighttime experiment: 9:00, 10:00, and 11:00 P.M. vs. 1:00, 2:00, and 3:00 A.M.) and the between-subject factor experiment (daytime bright light exposure vs. nighttime bright light exposure). The factor time is needed to include the three data points within the interval before the light condition and the three data points during the light condition. To answer the question whether light per se has an effect on psychological and physiological parameters, the effect of the interaction between condition and exposure is the relevant measure. It tells us whether the variable under study changes during light exposure relative to the preceding dim interval and whether this change differs from the condition in which no light was applied at all. To answer the question of whether the effect of light is dependent on time of day, the interaction effect of condition, exposure, and experiment was determined. Where interactions contributed significantly to the explained variance, post hoc ANOVAs were calculated to determine the direction of the effect.

RESULTS

Figure 2 shows the results of daytime (*left*) vs. nighttime (*right*) bright light exposure for the physiological variables heart rate, cortisol, and CBT. Figure 2, *top*, shows the changes in heart rate for the two experiments, before and during the light exposure. There was an effect of light on heart rate [interaction effects for the factors condition and exposure,
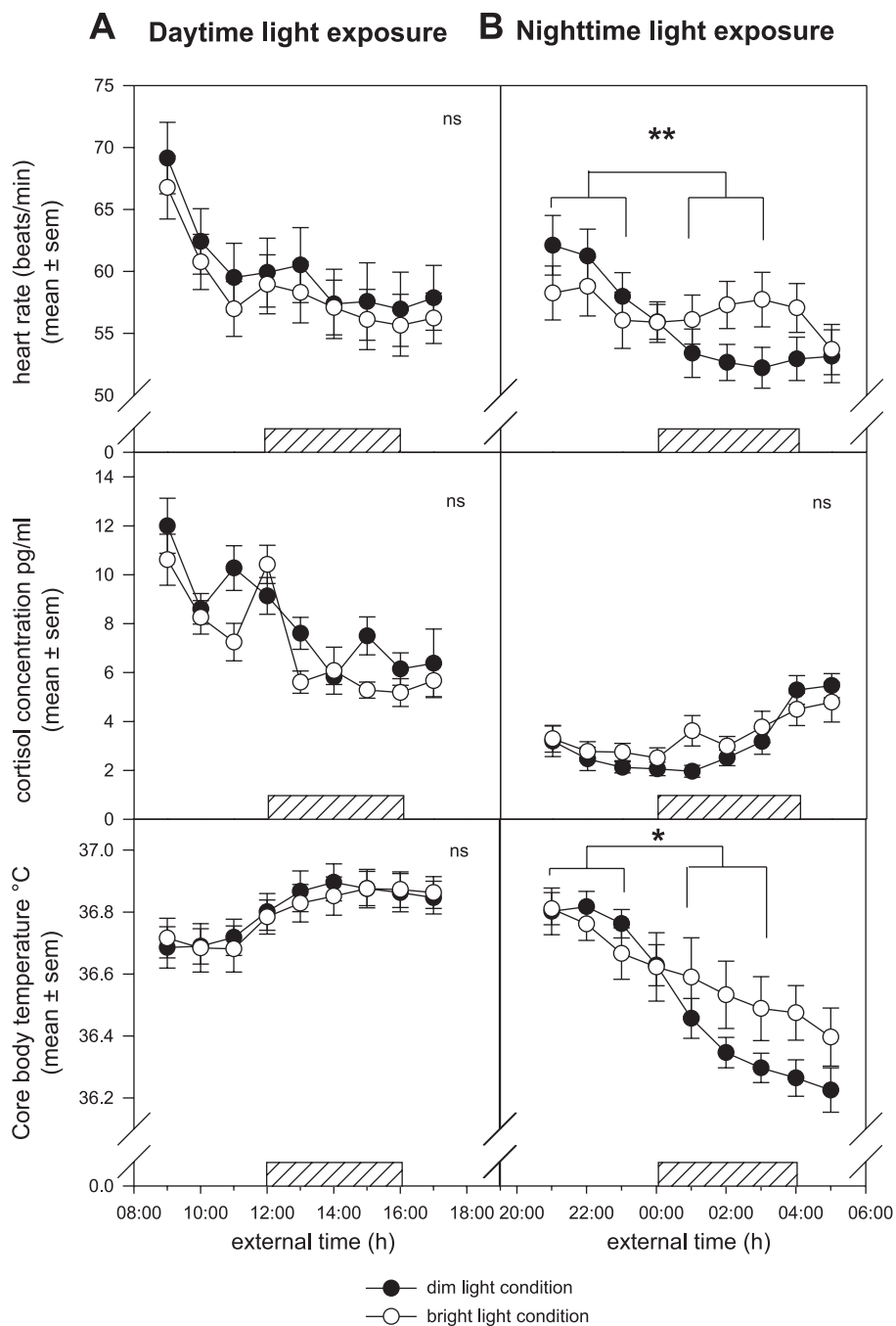
Fig. 2. Course of heart rate, cortisol concentration, and core body temperature for the two experiments, before and during bright light exposure vs. dim light. Hatched bars, period of light exposure (daytime experiment: noon until 4:00 P.M.; nighttime experiment: midnight until 4:00 A.M.). Repeated-measures ANOVA for the 3 h before (daytime experiment: 9:00, 10:00, and 11:00 A.M.; nighttime experiment: 9:00, 10:00, and 11:00 P.M.) vs. during the experimental condition (daytime experiment: 1:00, 2:00, and 3:00 P.M., nighttime experiment: 1:00, 2:00, and 3:00 A.M.) revealed a significant condition effect of the bright light on heart rate ($P = 0.010$) and core body temperature ($P = 0.017$), depending on the time of day, but no effect on cortisol ($P = 0.727$). Significances indicated refer to post hoc ANOVAs for the daytime and nighttime experiments separately (*$P < 0.05$ and **$P < 0.01$). NS, not significant.

$F_{(1,22)} = 13.0$, $P = 0.002$]. This effect depended on the time of day [3-way interaction of the factors condition, exposure, and experiment, $F_{(1,22)} = 7.9$, $P = 0.010$]. Post hoc ANOVAs showed that bright light exposure significantly increased heart rate during nighttime [$F_{(1,11)} = 22.9$, $P = 0.001$] but not during daytime [$F_{(1,11)} = 0.2$, $P = 0.604$].

Figure 2, *middle*, shows the cortisol concentration for both experiments, before and during the light exposure. Light had no significant effect on cortisol [interaction effect for the factors condition and exposure, $F_{(1,22)} = 0.9$, $P > 0.1$], independent of the time of day [3-way interaction for the factors condition, exposure, and experiment, $F_{(1,22)} = 0.1$, $P > 0.1$].

Figure 2, *bottom*, shows the courses of CBT during the two experiments, before and during the light exposure. As for heart rate, there was an overall effect of light on CBT [interaction effect for condition and exposure, $F_{(1,15)} = 4.5$, $P = 0.05$], and this effect of light did depend on the time of day [$F_{(1,15)} = 7.2$, $P = 0.017$]. Post hoc ANOVAs revealed that CBT increased in bright light exposure compared with dim light during nighttime [$F_{(1,6)} = 6.1$, $P = 0.048$] but not during daytime [$F_{(1,9)} = 0.3$, $P = 0.586$].

In Fig. 3 the effects of daytime (*left*) and nighttime (*right*) bright light exposure on the three psychological variables sleepiness, fatigue, and energy are depicted. Figure 3, *top*, shows a clear reduction of subjective sleepiness as measured
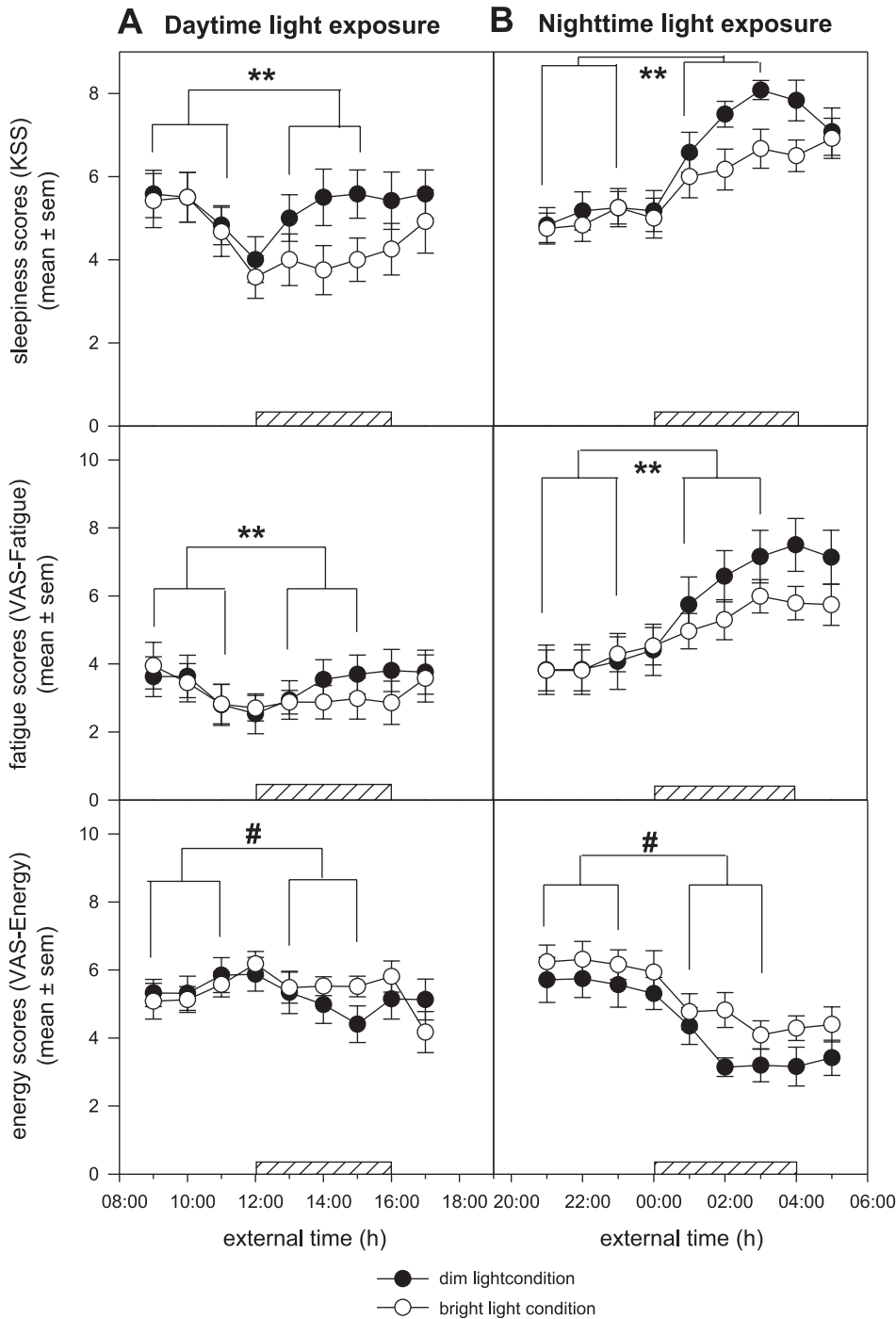
Fig. 3. Course of subjective sleepiness, fatigue, and energy for the two experiments, before and during bright light exposure vs. dim light. Hatched bars, period of light exposure (daytime experiment: noon until 4:00 P.M.; nighttime experiment: midnight until 4:00 A.M.). Repeated-measures ANOVA for the 3 h before (daytime experiment: 9:00, 10:00, and 11:00 A.M.; nighttime experiment: 9:00, 10:00, and 11:00 P.M.) vs. during (daytime experiment: 1:00, 2:00, and 3:00 P.M.; nighttime experiment: 1:00, 2:00, and 3:00 A.M.) the experimental condition revealed a significant condition effect of the bright light on sleepiness ($P = 0.001$) and fatigue ($P = 0.008$) and a trend for energy ($P = 0.071$). The effects turned out to be independent of the time of day (**$P < 0.01$ and #$P < 0.1$)

by the KSS for the daytime and nighttime bright light exposure [interaction effect for the factors condition and exposure, $F_{(1,22)} = 16.8$, $P < 0.001$]. This alerting effect of bright light exposure is independent of the time of day at which light is presented [3-way interaction effect for the factors condition, exposure, and experiment, $F_{(1,22)} = 0.4$, $P = 0.527$].

The course of subjective fatigue as measured by the VAS-F during daytime and nighttime bright light exposure follows a similar pattern as subjective sleepiness, i.e., subjects in the bright light group report that they feel less fatigued during the light exposure than before compared with the dim light group [interaction effect for factors condition and exposure, $F_{(1,22)} = 8.3$, $P = 0.008$]. As for subjective sleepiness, the effect of bright light on subjective fatigue is independent of time of day [3-way interaction of condition, exposure, and experiment, $F_{(1,22)} = 0.8$, $P = 0.372$]. Figure 3, *bottom*, depicts the course of the subjective feeling of energy as measured by the VAS-E for the daytime and nighttime experiment, before and during the light exposure. As expected, the energy ratings show the reversed pattern of subjective sleepiness and fatigue, i.e., in both experiments the subjects report on average to feel more energetic during

the light exposure in the bright light condition than in the dim light condition. This interaction effect of condition and exposure was not significant [$F(1,22) = 3.6$, $P = 0.071$]. Again the effect was independent of the time the light was given [$F(1,22) = 0.4$, $P = 0.503$].

DISCUSSION

To answer the question of which effects of bright light exposure on human psychophysiology are time-of-day dependent, we compared 4 h of daytime with 4 h of nighttime bright light exposure on heart rate, cortisol, CBT, sleepiness, fatigue, and energy. The data were collected in two different groups of subjects, one being exposed to light during the day and one during the night. The groups had similar sleep durations but differed slightly in their preferred sleep timing. The subjects were instructed to sleep between midnight and 8:00 A.M. during the week before the experiments. Therefore, it is unlikely that the results are because of differences between the two groups.

Concerning the physiological variables heart rate and CBT, we found an overall effect of light that was time-of-day dependent, i.e., nighttime bright light exposure increased heart rate and reduced the circadian drop in CBT, whereas daytime bright light exposure increased neither heart rate nor CBT. The heart rate results are in accordance with the results of Scheer et al. (48) who showed an increase in heart rate in response to bright light (20 min of 100 and 800 lux) during the nighttime (20 h after habitual wake time, range of wake time: 6:15–8:30 A.M.) and no effect on heart rate during daytime. Cajochen and colleagues (10) exposed their subjects from 9:30 to 11:30 P.M. to short-wavelength light (460 nm) and found an increase in heart rate. They also found an increase of CBT that resembles our current results and the finding of Badia et al. (5) that nighttime bright light exposure elevates CBT.

The lack of effects of bright light on cortisol concentrations during the daytime might be because of our timing of the light exposure. In our study, the light exposure period was from noon until 4:00 P.M., with no effect on the cortisol, whereas the following studies induced an increase in cortisol with an earlier timed period of light exposure. Leproult et al. (33) exposed their subjects from 5:00 to 8:00 A.M. to 4,000 lux of bright light, Scheer and Buijs (47) between 5:45 and 7:30 A.M. to 1 h of 800 lux, and Thorn et al. (49) used a dawn simulator (250 lux over 30 min) during awakening (mean awakening time: 6:40 A.M.) to increase cortisol, with all periods of exposure in the range of the morning cortisol peak (31). The absence of an effect of bright light on cortisol concentrations during the nighttime is not surprising, since cortisol production is usually low at that time. The literature on the effects of nighttime bright light on cortisol is inconclusive, since, e.g., Kostoglou-Athanassiou et al. (28) found a reduction of cortisol after they exposed their subjects to 6 h of bright light, whereas Leproult and coworkers (34) found no effect of bright light exposure on the cortisol concentrations of their subjects.

We found no time-of-day-dependent effect of light on the three (related) psychological variables we measured (sleepiness, fatigue, and energy). It certainly is possible that the similarity of the sleepiness suppressive effects of light in the night and during the day partially results from the increased

sleep pressure due to restricted sleep duration (7 h) on the adaptation night in *experiment A*. Yet, many people restrict sleep duration to 7 h or less, especially on work days (51). Hence, in terms of sleepiness during the daytime, the situation in *experiment A* is certainly not unusual. The similarity of the sleepiness-reducing effects of daytime and nighttime light exposure means that bright light elicited its alerting and sleepiness-reducing properties independent of the timing of exposure. Because of the fact that there is almost no melatonin secreted during daytime (33, 42, 43), which therefore cannot be suppressed by light, this means that there must be an alternative mechanism or pathway by which light immediately influences alertness in humans. Despite the results of Kräuchi and colleagues (29, 30) showing a functional link between the degree of heat loss (distal vasodilatation) and subjective sleepiness (measured by the KSS), we found a reduction of subjective sleepiness in the absence of any effect of daytime light on CBT, indicating again that light affects human alertness in another way besides the mechanisms of melatonin suppression and/or elevation of CBT.

Evidence in favor of such an alternative pathway of light-altering psychological states comes from neuroanatomical animal studies that show indirect projections from the SCN to brain areas that are strongly associated with the regulation of sleep-wake processes. Aston-Jones et al. (2) found a neural circuit in the rat that proved the locus coeruleus to be a target area of indirect projections from the SCN via the dorsomedial hypothalamic nucleus. By performing lesions of the dorsomedial hypothalamic nucleus, which eliminated circadian variations in the locus coeruleus, they showed the functionality of this circuit. The locus coeruleus is associated with sleep-wake regulatory processes (36). Recently, Deurveilher and colleagues (19, 20) showed that the medial preoptic area, the subparaventricular zone, and the dorsomedial hypothalamic nucleus might not only serve as relays to sleep-promoting nuclei, such as the ventrolateral and the medial preoptic nuclei, but also to wake-regulatory brain areas, such as the locus coeruleus. Furthermore, Lu et al. (37) identified a set of sleep-active cells in the ventrolateral preoptic nucleus of rats that receive direct luminance signals from the retina. The ventrolateral preoptic nucleus also belongs to the target regions for the projections from intrinsically photosensitive retinal ganglion cells, which contribute to circadian entrainment, pupillary light reflex, and the regulation of sleep-wake states (23). In humans, the locus coeruleus appears to be one of the possible candidate nuclei that was influenced by bright light exposure during the nighttime as Perrin and colleagues (41) showed in their positron emission tomography study using regional blood flow as a activation-deactivation marker of brain areas.

Concerning the primary question as to what extent immediate effects of bright light on human psychophysiology are time-of-day dependent, we conclude that the measured effects on the psychological variables during daytime are not significantly different from those during nighttime bright light exposure. This cannot simply be explained by the changes in heart rate and CBT, because these variables do not change in any systematic way in response to light during the daytime.

We are aware that our comparison includes only two circadian phases and a limited number of variables. Yet, the results clearly demonstrate that psychological responses to light are

similar when comparing light exposures around midnight with midday, whereas physiological variables thought to be related to those psychological reactions behave quite differently. Apparently, the regulation of human alertness is more complex than has been estimated so far. Given the importance of alertness for performance, the mechanisms behind these differential light effects need to be discovered.

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