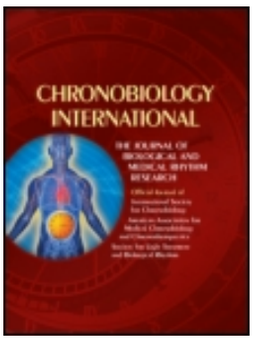

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A COMPROMISE PHASE POSITION FOR PERMANENT NIGHT SHIFT WORKERS: CIRCADIAN PHASE AFTER TWO NIGHT SHIFTS WITH SCHEDULED SLEEP AND LIGHT/DARK EXPOSURE

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Night shift work is associated with a myriad of health and safety risks. Phase-shifting the circadian clock such that it is more aligned with night work and day sleep is one way to attenuate these risks. However, workers will not be satisfied with complete adaptation to night work if it leaves them misaligned during days off. Therefore, the goal of this set of studies is to produce a compromise phase position in which individuals working night shifts delay their circadian clocks to a position that is more compatible with nighttime work and daytime sleep yet is not incompatible with late nighttime sleep on days off. This is the first in the set of studies describing the magnitude of circadian phase delays that occurs on progressively later days within a series of night shifts interspersed with days off. The series will be ended on various days in order to take a "snapshot" of circadian phase. In this set of studies, subjects sleep from 23:00 to 7:00 h for three weeks. Following this baseline period, there is a series of night shifts (23:00 to 07:00 h) and days off. Experimental subjects receive five 15 min intermittent bright light pulses ($\sim$3500 lux; $\sim$1100 $\mu W/cm^2$) once per hour during the night shifts, wear sunglasses that attenuate all visible wavelengths—especially short wavelengths ("blue-blockers")—while traveling home after the shifts, and sleep in the dark (08:30–15:30 h) after each night shift. Control subjects remain in typical dim room light ($<$50 lux) throughout the night shift, wear sunglasses that do not attenuate as much light, and sleep whenever they want after the night shifts. Circadian phase is determined from the circadian rhythm of melatonin collected during a dim light phase assessment at the beginning and end of each study. The sleepiest time of day, approximated by the body temperature minimum (T_{min}), is

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estimated by adding 7 h to the dim light melatonin onset. In this first study, circadian phase was measured after two night shifts and day sleep periods. The T_{min} of the experimental subjects (n = 11) was 04:24 ± 0.8 h (mean ± SD) at baseline and 7:36 ± 1.4 h after the night shifts. Thus, after two night shifts, the T_{min} had not yet delayed into the daytime sleep period, which began at 08:30 h. The T_{min} of the control subjects (n = 12) was 04:00 ± 1.2 h at baseline and drifted to 4:36 ± 1.4 h after the night shifts. Thus, two night shifts with a practical pattern of intermittent bright light, the wearing of sunglasses on the way home from night shifts, and a regular sleep period early in the daytime, phase delayed the circadian clock toward the desired compromise phase position for permanent night shift workers. Additional night shifts with bright light pulses and daytime sleep in the dark are expected to displace the sleepiest time of day into the daytime sleep period, improving both nighttime alertness and daytime sleep but not precluding adequate sleep on days off.

Keywords Night shift work, Light, Sleep, Human, Circadian rhythms, Melatonin

INTRODUCTION

Night shift workers are often sleepy, inefficient, and prone to accidents while working (Akerstedt, 1988; Dinges, 1995; Folkard and Lombardi; 2004 Mitler et al., 1988; Santos et al., 2004; Smith et al., 1994; Torsvall et al., 1989), and they often have difficulty maintaining sleep during the day after work (Akerstedt, 1995; Kogi, 1985; Tilley et al., 1982). These problems, attributed to circadian misalignment, have been reduced or eliminated in simulated and real night shift studies by shifting circadian rhythms to align with the desired day sleep and night work schedule, usually with the help of bright light (for reviews, see Boivin and James, 2005; Burgess et al., 2002; Eastman and Martin, 1999; Revell and Eastman, 2005). The complete re-alignment or re-entrainment of circadian rhythms to the unusual schedule is not necessary to produce significant physiological adaptation to night work (Crowley et al., 2004). We define circadian adaptation as phase delaying the sleepiest time of day, usually estimated by the temperature minimum (T_{min}), at least until it occurs during the daytime sleep period (Eastman and Martin, 1999).

A previous simulated night work study (Crowley et al., 2003) tested combinations of 1) intermittent bright light during the night shift (23:00–07:00 h), 2) normal or very dark sunglasses during the commute home, and 3) fixed daytime dark/sleep episodes (08:30–15:30 h) to produce circadian adaptation. Each subject was categorized based on where his or her final T_{min} occurred after five consecutive night shifts relative to the previous daytime sleep episode: not re-entrained (T_{min} before daytime sleep, before 08:30 h), partially re-entrained (T_{min} within the first half of daytime sleep, between 08:30 and 12:00 h), and completely re-entrained (T_{min} within the second half of daytime sleep, between

12:00 and 15:30 h). The melatonin rhythm is a more reliable phase marker of the circadian clock than the temperature rhythm (Benloucif et al., 2005; Klerman et al., 2002); so the final phase position in this study was analyzed by measuring the dim light melatonin onset (DLMO). The sleepiness peak was then calculated by adding 7 h to the DLMO because the T_{min} occurs approximately seven hours after the DLMO (Benloucif et al., 2005; Brown et al., 1997; Eastman et al., 2000; Mongrain et al., 2004; Sharkey and Eastman, 2002). Performance, alertness, and mood during the night shift were improved in those subjects who achieved partial or complete re-entrainment compared to those who were not re-entrained, but there were no differences between partial and complete re-entrainment (Crowley et al., 2004). Because real night shift workers might have difficulty adapting to a normal nighttime sleep schedule on days off if they are completely re-entrained to the night-work/day-sleep schedule, the best compromise may be partial re-entrainment, delaying the sleepiest time of day into the beginning of daytime sleep. In this case, performance and alertness will be improved during the night shift; yet, the sleepiness peak will still fall at the end of nighttime sleep on days off, given a fairly late sleep schedule.

The present authors have previously proposed bright light and sleep schedules for permanent night work that are designed to produce and maintain partial re-entrainment in what is called a *compromise phase position* (see Figure 5 in Eastman and Martin, 1999, and Figure 4 in Burgess et al., 2002). A compromise phase position is one in which the circadian clock is delayed enough to displace the peak time of sleepiness into the daytime sleep period when working night shifts while still allowing this time of peak sleepiness to occur late in the sleep period on days off. The authors are in the process of testing such a schedule using several series of night shifts alternating with days off spanning about two weeks. They will determine whether the compromise phase position can be achieved and maintained and whether baseline levels of sleep, performance, and alertness can also be maintained. "Snapshots" will be taken of the circadian phase on various days during the sequence, some after a series of night shifts and some after days off, by stopping the sequence to collect full melatonin profiles. One purpose of this report is to provide a detailed account of the methods that will be used throughout this multi-part study. In addition, data from the first snapshot taken after two consecutive night shifts will be reported.

In the previous study outlined above (Crowley et al., 2003), circadian phase prior to working night shifts was an important factor contributing to the extent of adaptation to night work. Baseline T_{mins} (DLMOs + 7 h) before the time of the commute home hindered phase delays, while T_{min} falling after the commute home facilitated phase delays, presumably due to when morning sunlight exposure occurred relative to the individuals'

circadian phase. Therefore, this series of studies will focus on those individuals with T_{mins} before the commute home, who cannot as easily achieve circadian adaptation. To achieve this baseline circadian phase, subjects are scheduled to sleep from 23:00 to 07:00 h on weeknights during three weeks of baseline conditions.

In this series of studies, experimental subjects are exposed to intermittent bright light pulses at fixed times during each night shift and are required to be in bed in the dark at home trying to sleep for specified hours following each night shift and on days off. The bright light at night and regular sleep/dark period soon after each night shift are designed to facilitate adaptation to the night shift schedule. Control subjects remain in typically dim room light throughout the night shifts and are allowed to sleep whenever they want after the night shifts and during days off. This sleep and light exposure pattern is similar to what most real night shift workers experience and is not conducive for phase delaying the circadian clock for adaptation to a night shift schedule.

The present study took a "snapshot" after only two simulated night shifts and two day sleeps, before the experimental subjects were expected to achieve the compromise phase position, to check that their circadian rhythms were delaying as expected. Given the baseline sleep schedule from 23:00 to 07:00 h, the baseline DLMO was expected to be around 21:00 h, as previously demonstrated (Revell et al., 2005) and the estimated T_{min} to therefore be around 04:00 h (21:00 h + 7 h). In previous studies using bright light during the night shift, the circadian clock phase delayed approximately 2 h/day (Eastman, 1992; Eastman and Martin, 1999). Therefore, the T_{min} of the experimental group was expected to delay a total of 4 h and be around 08:00 h after the second night shift, not quite within the daytime sleep period that started at 08:30 h. The T_{min} of the control group was expected to remain at about the same phase position, not showing significant phase delays.

MATERIALS AND METHODS

Subjects

Twenty-four subjects completed the study, but one male subject was excluded from analysis due to low melatonin levels. Of the remaining 23 subjects, 11 (5 males, 6 females, mean age $\pm$ SD = 24.5 $\pm$ 3.3 yrs) were in the experimental group and 12 (6 males, 6 females, 29.8 $\pm$ 8.9 yrs) were in the control group. Subjects did not report any medical, psychiatric, or sleep disorders as assessed by a telephone interview, an in-person interview, and several screening questionnaires (i.e., the Health Information Questionnaire [derived from Tasto et al., 1978]; the Minnesota

Multiphasic Personality Inventory-2 [Butcher et al., 1989]; the Epworth Sleepiness Scale [Johns, 1991]; and the Pittsburgh Sleep Quality Index [Buysse et al., 1989]). All subjects had body mass indices $\leq 30\ kg/m^2$, were non-smokers, drank <300 mg of caffeine/day, and were free from prescription medications, except for three female subjects who took oral/injectable contraceptives. Subjects were also free from recreational drug use as confirmed by a urine toxicology screen at the start of the study. Subjects had not worked a night shift three months prior nor traveled across more than three time zones one month prior to starting the study. Nine of the 23 subjects had worked night shifts at some point before enrolling in the study (four subjects in the experimental group, and five subjects in the control group). The Rush University Medical Center Institutional Review Board approved the study, and it adhered to the ethical standards of this journal (Touitou et al., 2004). All subjects gave written informed consent and were paid for their participation.

Design

This was a between-subjects design with two groups: an experimental group and a control group. Subjects participated in sets of four, and each set was randomly assigned to either the experimental or control group.

Baseline Sleep and Morning Light Schedule

During weeknights, subjects in both groups were required to sleep (or, if they could not sleep, to remain in bed) in the dark from 23:00 to 07:00 h. During the weekends (Friday and Saturday nights), they could go to bed between 23:00 h and midnight and wake up between 07:00 and 08:00 h. After waking each morning, subjects were required to go outside for at least 15 min between 08:00 and 09:00 h. This simulated the outdoor light most day workers are exposed to while commuting to work. The study occurred during the summer and fall months (July–October).

Napping was permitted on Saturday and Sunday afternoons between 13:30 and 16:30 h, a 3 h zone centered 12 h from the midpoint of the nocturnal sleep period on weeknights. All subjects adhered to this sleep schedule for 15 consecutive days before coming into the lab for the baseline phase assessment. They then resumed the baseline sleep schedule for six additional days before returning to the lab for two simulated night shifts. Figure 1 illustrates the protocol and includes the sleep times for subjects in the experimental group.

To ensure that the phase position measured during the baseline phase assessment could be used as an accurate estimate of phase one week later, a study examining the reproducibility of three circadian phase markers—the

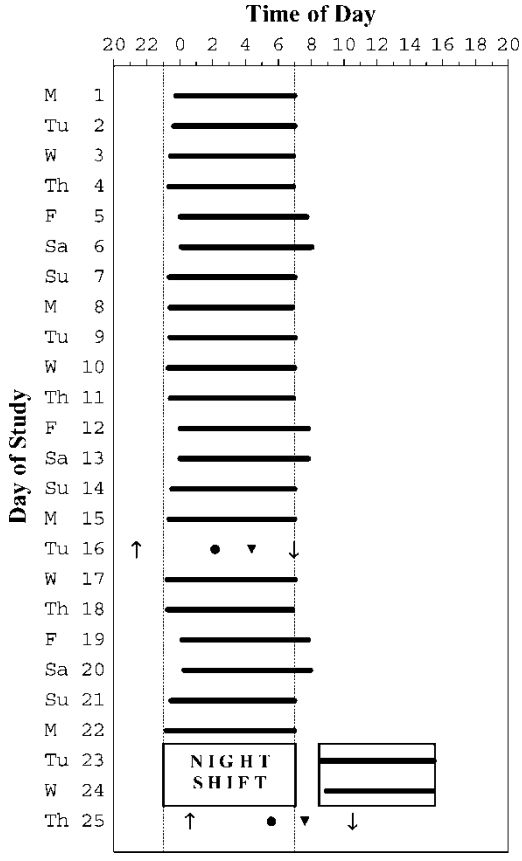

FIGURE 1 Protocol and results for the experimental group. Black bars depict the average sleep onset and wake times, according to daily sleep logs. Dashed lines at 23:00 and 07:00 h represent the week-night sleep schedule during baseline. Subjects were permitted to go to sleep and wake up 1 h later on weekends. The rectangle from 08:30 to 15:30 h on days 23 and 24 outlines the period when subjects were required to remain in bed in the dark. Circadian phase assessments occurred on day 16 (baseline) and 25 (final). Average DLMO (↑), midpoint (●), and DLMOff (↓) were measured during each phase assessment. The T_{min} (▼) was calculated by adding 7 h to the DLMO.

DLMO, the dim light melatonin offset (DLMOff), and the midpoint between the DLMO and DLMOff—was conducted with phase assessments one week apart (Revell et al., 2005). Subjects adhered to a baseline sleep and morning outdoor light schedule identical to what is used in the current study. The absolute phase changes (i.e., the average change in phase between the two phase assessments, regardless of direction), which are the best indicators of reproducibility, were small: 34, 20, and 24 mins for the DLMO, midpoint, and DLMOff, respectively. These findings justified using the circadian phase determined from the baseline phase assessment as an estimation of phase immediately before the first night shift in all the studies of this series.

Sunglasses

All subjects wore sunglasses when outside during the day, including on the way home from the night shifts. Experimental subjects wore sunglasses with black Bandit frames and espresso "blue-blocker" lenses (0 to about 25% transmission, Uvex Safety, Smithfield, RI, USA; see Figure 2a). According to Uvex specification sheets (http://www.uvex.com/pdf/lenscharts/espresso.pdf), these lenses block 97% of blue light and are recommended for driving and most outdoor activities. Control subjects wore sunglasses with copper Bandit frames and custom "light" espresso lenses (0 to about 55% transmission; see Figure 2b).

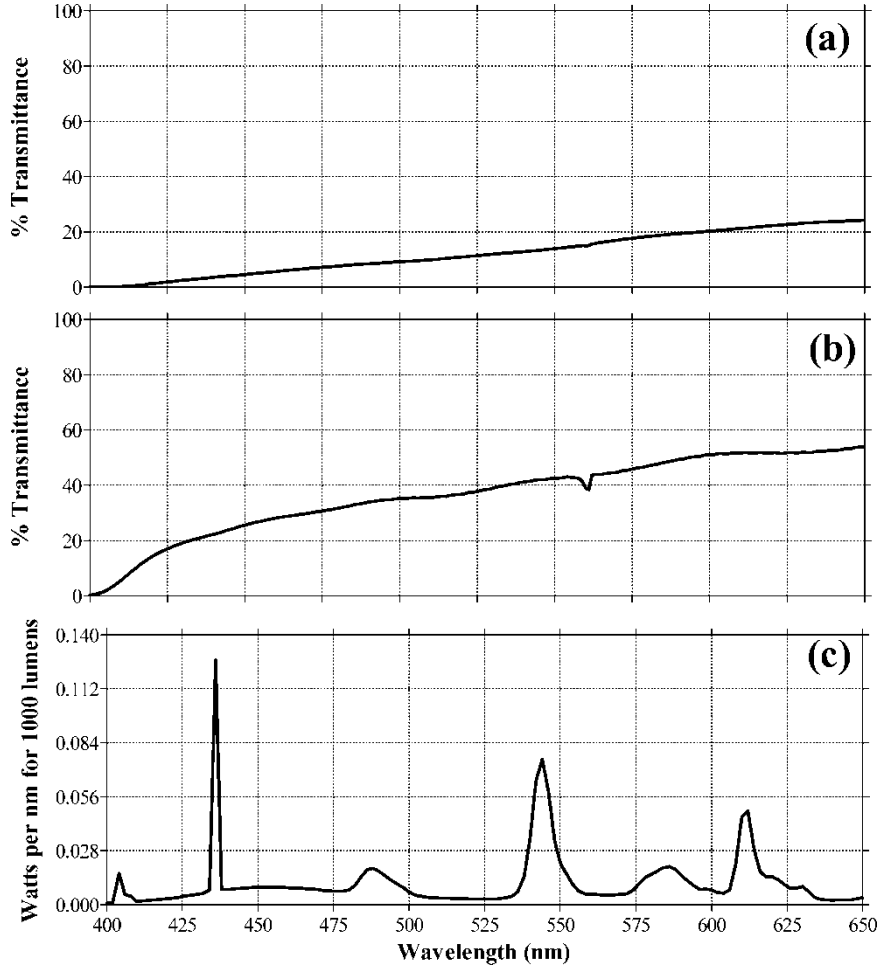

FIGURE 2 Spectral plots from 400 to 650 nm of (a) light transmission of espresso lenses worn by experimental subjects, (b) light transmission of "light" espresso lenses worn by control subjects, and (c) output of SunRay lamps used during night shifts (experimental group only).

Night Shift Light

All subjects came to the lab for two simulated night shifts, from 23:00 to 07:00 h on days 23 and 24. Experimental subjects were exposed to five 15 min pulses of bright light during each night shift. These pulses ended at 01:00, 02:00, 03:00, 04:00, and 05:00 h, and were designed to coincide with the delay portion of the light phase response curve (PRC). In the authors' most recent PRC (Revell and Eastman, 2005), the crossover point between delays and advances occurs about 8 h after the DLMO. Thus, given a baseline DLMO of 21:00 h, which was expected given the authors' previous study with the identical baseline sleep schedule (Revell et al., 2005), the light pulses would occur before the crossover point at 05:00 h. These light pulses occurred at the same clock time on each night shift, which is in contrast to the previous study (Crowley et al., 2003) in which light pulses were gradually delayed on successive night shifts. While the moving light pattern can produce larger phase delays, the stationary light pattern is intended to produce smaller phase delays, which should be better for maintaining a compromise phase position. It would also be easier to implement in real night work.

Four light boxes (SunRays; 58.4 cm × 39.4 cm × 8.3 cm; The SunBox Company Inc., Gaithersburg, Md., USA) were placed in adjustable floor stands and set around the perimeter of a large, round table (152 cm diameter). Each of the light boxes was directed toward the middle of the table and angled down, $\sim 33^{\circ}$ from the vertical. The middle of each light box was $\sim$52 cm above the tabletop. Each light box had a transparent prismatic diffuser screen (56.2 cm × 31.8 cm) and contained four non-UV fluorescent lamps (Sylvania FBO31/50K, 5095 K, Danvers, Mass., USA). The spectral plot of these lamps is shown in Figure 2c. Subjects sat in spaces between the light boxes around the table such that each subject faced two light boxes across the table and received peripheral light from the two adjacent light boxes. The light intensity, measured periodically at the angle of gaze by an Extech 401025 light meter (Waltham, Mass., USA), ranged from 3000 to 5910 lux. The total irradiance measured at the typical angle of gaze by an IL1400 radiometer and SEL-033/F/W detector (International Light, Inc., Newburyport, Mass., USA) was $\sim 1100\ \mu W/cm^2$. The irradiance from the blue portion of the spectrum (400–490 nm) calculated using a SCS490 sharp cut filter was $267\ \mu W/cm^2$. Subjects were exposed to $\sim 2.9 \times 10^{15}$ photons/cm^2/sec, of which $\sim 7.4 \times 10^{14}$ photons/cm^2/sec was between 400–490 nm. In between the pulses of bright light, experimental subjects remained in dim room light. Lighting of $<$50 lux in the angle of gaze was controlled by a dimmer switch and provided by three ceiling fixtures, each containing three fluorescent lamps (4100 K). The control subjects remained in the dim room light throughout the night shifts. The light intensity the control subjects

are exposed to during the night shifts, though dim, is not unlike what some real night shift workers experience during their shifts.

Daytime Sleep and Afternoon Light Schedule

Following each night shift, experimental subjects were required to go home and remain in bed, trying to sleep, from 08:30 to 15:30 h. Control subjects were allowed to sleep whenever they wanted. Upon waking in the afternoon, experimental subjects were required to go outside for at least 15 mins between 15:30 and 17:30 h.

To ensure that experimental subjects were in the dark from 08:30 to 15:30 h, their bedroom windows were covered with thick, black plastic. We also installed a window air conditioner in their bedroom, if they did not already have air conditioning, because bedrooms with black plastic over the windows become uncomfortably hot for sleeping in the daytime in the summer months. The control subjects were offered air conditioners as well.

Circadian Phase Assessments

Subjects stayed overnight and remained awake in dim light (<5 lux) watching TV or playing video games while seated in comfortably padded recliners. Post-study irradiance measured at eye level with the television on ranged from 2.26 to 3.80 $\mu W/cm^2$, depending upon the angle of gaze. The blue spectrum (400–490 nm) irradiance ranged from 0.66 to 1.38 $\mu W/cm^2$.

During the phase assessments, subjects gave a saliva sample using a Salivette with cotton insert (Sarstedt, Newton, NC, USA) every 30 min. Sampling for the baseline phase assessment (day 16) started at 15:30 h and ended at 12:00 h; the final phase assessment (day 25) started and ended at 18:00 h. Each sample was centrifuged immediately upon collection and frozen. These samples were later shipped with dry ice to Pharmasan Labs (Osceola, Wisc., USA) and radioimmunoassayed for melatonin. All samples from an individual subject were assayed together. The sensitivity of the assay was 0.7 pg/ml; the intra- and inter-assay variability was 12.1% and 13.2%, respectively. Small snacks and drinks were provided throughout the session, but subjects were not permitted to eat or drink during the 10 min before each sample. Just prior to this 10 min interval, if they had eaten anything, they had to brush their teeth with a soft toothbrush and water while remaining seated; if they drank anything other than water, they had to rinse their mouth with water. Washroom trips were strongly discouraged during this 10 min interval. The washroom and adjoining hallway were dimly lit (<5 lux). To further ensure the most accurate melatonin levels from the assays, alcohol and non-steroidal

anti-inflammatory drugs (NSAIDs) were prohibited 24 h before and during the phase assessments, and caffeine, chocolate, and bananas were prohibited 6 h before and during the phase assessments. Subjects also could not use toothpaste, mouthwash, or lipstick during the phase assessments.

Additional Procedures

Subjects kept daily sleep, light, and event logs throughout the study. For each sleep period, subjects reported bedtime, estimated sleep onset time, awakening from sleep for >5 min, wake time, and the time of getting out of bed. In addition, they were required to call the lab's voice mail system just before going to bed each night and immediately upon waking each morning. On daily light logs, subjects recorded the times they went outside during the day and whether or not they were wearing the sunglasses mentioned previously. Subjects also recorded all caffeine, alcohol, and over-the-counter medication consumption on daily event logs. They were restricted to <300 mg of caffeine (<about three 8 oz cups of coffee) and <2 alcoholic drinks each day, except before and during phase assessments, when these were prohibited. Caffeine was not permitted after 17:00 h each day during baseline or when subjects were in the lab for a night shift. Experimental subjects were also not allowed caffeine in the interval between the end of a night shift (07:00 h) and the start of daytime sleep (08:30 h). Compliance with caffeine and alcohol restrictions could not be strictly enforced when subjects were outside of the laboratory, but subjects were breathalyzed upon arrival at the lab before night shifts and phase assessments.

Monitoring Subject Compliance

Subjects wore two Actiwatch-L (AW-L) devices (Mini Mitter, Bend, Oreg., USA). One was worn around the non-dominant wrist to measure movement, and the other around the neck with a cord to measure ambient light. The AW-L worn as a medallion around the neck captured light intensity at eye level more accurately than that worn around the wrist. Both AW-Ls were worn throughout the study, but the one around the neck was removed while showering and sleeping. Before going to bed, subjects placed the medallion AW-L with the photosensor face-up on a surface at eye level near the bed; before showering, subjects placed it face-up on a flat surface in the bathroom. To ensure compliance to the sleep and light schedule, actigraphy and photosensor data were examined and compared against daily sleep and light logs every 2–3 days throughout the study.

Data Analysis

Summary statistics are presented as means and standard deviations unless otherwise indicated.A two-tailed significance level of .05 was used.

Circadian Phase

Each melatonin profile was smoothed with a locally weighted least squares (LOWESS) curve (Chambers et al., 1983; Cleveland, 1979) generated by GraphPad Prism, using the "fine" setting. As in the present authors' previous studies (Revell et al., 2005, 2006), the threshold for each profile was calculated by taking the average of the five lowest, consecutive raw data points at the beginning of the profile and adding 15% of the average of the five highest, consecutive raw data points in the profile. The DLMOs were defined as the time when melatonin levels in the smoothed curve crossed and stayed above the threshold for at least two successive hours. The DLMOffs were defined as the time when melatonin levels in the smoothed curve crossed and stayed below the threshold for at least 25 successive minutes. This method for calculating the DLMO and DLMOff takes into account differences in the amplitude of the absolute levels of melatonin, which vary substantially between subjects. In contrast to the DLMO20% (e.g., Benloucif et al., 2005) or DLMO25% (e.g., Santhi et al., 2005) method, this threshold is typically lower on a melatonin profile (i.e., closer to the actual time of melatonin secretion onset), but above the low daytime background level of melatonin.

The phase shifts were analyzed with a repeated measures multivariate analysis of variance (MANOVA). Dependent variables were: DLMO, midpoint, and DLMOff. The between-subjects factor was group (experimental and control) and the within-subjects factor was time (baseline and final). A significant MANOVA was followed by univariate analyses of variance (ANOVAs) on each phase marker.

The time of peak sleepiness, which is often estimated by the T_{min}, is also of interest, but here it is measured by the melatonin rhythm rather than the temperature rhythm. This is done because, as described in the Introduction, the melatonin rhythm is a more reliable marker of the phase of the circadian clock. The sleepiest time of day is estimated by adding 7 h to the DLMO, because the T_{min} occurs, on average, 7 h after the DLMO. This phase position, the DLMO + 7 h, is a more reliable phase position to mark a specific point in the circadian cycle than if temperature was measured directly. Whether the constant of 7 h is the best to add to pinpoint the sleepiest time of day is a subject for future research.

Sleep

The total sleep duration for each sleep period was calculated from daily sleep logs:

(final wake time − sleep onset time) − (awakenings during sleep > 5 min).

Sleep duration during baseline (days 1 through 15) and after each night shift (days 23 and 24) was analyzed using a 2 × 3 repeated measures ANOVA. The between-subjects factor was group (experimental and control), and the within-subjects factor was day (baseline average, day 23, and day 24). Greenhouse-Geiser corrections were used to correct for violations of sphericity for the within-subjects effects. When a significant interaction was found, simple main effects analyses were conducted to determine the source of the interaction.

RESULTS

Circadian Phase

Baseline and final circadian phase markers are shown in Table 1. These phase markers were also illustrated in Figure 1, but only for the experimental group. The baseline DLMOs were about 21:00 h, as expected from the authors' previous study (Revell et al., 2005), and thus the T_{min} was about 04:00 h. The final T_{min} of the experimental group was 07:36 h, which was close to the target of 08:00 h. After two night shifts, the experimental group phase delayed more than 3 h, while the control group phase delayed less than 1 h (Figure 3). The MANOVA showed a significant time by group interaction [$F(3, 19) = 9.486$, $p < 0.001$]. Significant interactions were found in the associated ANOVAs for DLMO [$F(1, 21) = 25.241$, $p < 0.001$], midpoint [$F(1, 21) = 30.140$, $p < 0.001$], and DLMOff [$F(1, 21) = 22.962$,

TABLE 1 Circadian Phase Markers during Baseline and After Two Night Shifts. Values are Mean Clock Time (SD in hrs)

	Experimental		Control	
	Baseline	Final	Baseline	Final
DLMO	21:24 (.8)	0:36 (1.4)	21:00 (1.0)	21:48 (1.3)
Midpoint	2:12 (.8)	5:36 (1.4)	2:00 (.9)	2:54 (1.4)
T_{min}*	4:24	7:36	4:00	4:48
DLMOff	6:54 (1.2)	10:30 (1.8)	7:06 (1.0)	8:00 (1.6)

*Calculated by adding 7 h to the DLMO.

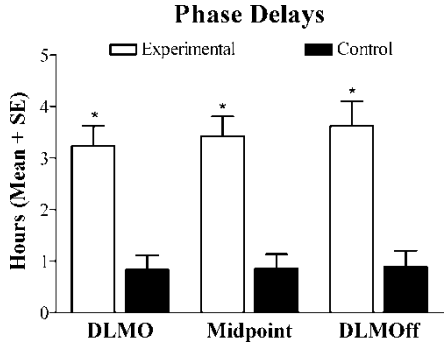

FIGURE 3 Circadian phase shifts from the baseline to final phase assessment for experimental (n = 11) and control (n = 12) subjects. * denotes significantly larger than control group, $p < .001$.

$p < 0.001$]. These results indicate that the experimental group phase delayed significantly more than the control group.

Sleep

All subjects adhered to the baseline sleep schedule. Figure 1 showed the average sleep times of subjects in the experimental group. Subjects in the control group slept at similar times on days 1–22, but, following the night shifts, they slept at various times (representative examples in Figure 4).

Both groups slept a little less after the first night shift (day 23) than during baseline (see Figure 5). This was expected because the sleep opportunity was less (only 7 h for day sleep compared to 8 h on weeknights and up to 9 h on weekends during baseline). There was not much difference between the two groups on day 23, but on day 24 (after the second night shift), the experimental group slept almost 2 h more than the

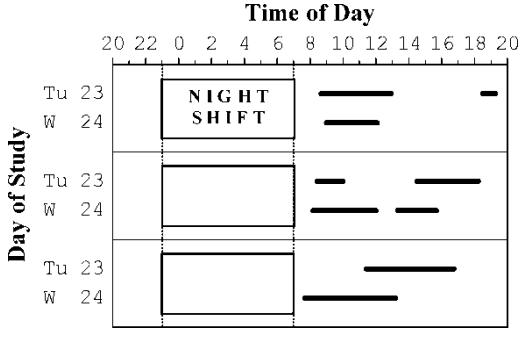

FIGURE 4 Sleep times of three representative control subjects on days 23 and 24, according to daily sleep logs. Black bars depict sleep times. Following the night shifts, control subjects were free to sleep whenever they wanted.

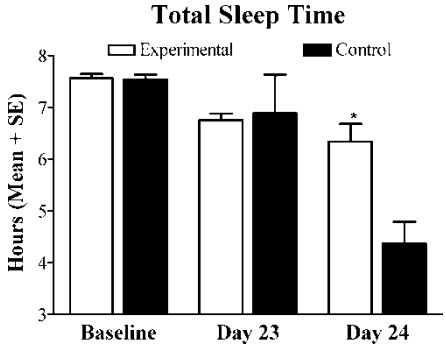

FIGURE 5 Average sleep duration calculated from daily sleep logs for experimental (n = 11) and control (n = 12) subjects during baseline (days 1 through 15) and following the first and second night shifts (days 23 and 24). * denotes significantly larger than control group, $p < .01$.

control group. A repeated measures ANOVA showed a significant time by group interaction [$F(1,28) = 4.314$, $p = 0.037$]. Simple main effects indicated that subjects in the experimental group slept significantly more than controls on day 24 ($p < 0.01$).

DISCUSSION

The circadian rhythms of the experimental group (with intermittent bright light during the night shifts, blue-blocker sunglasses during the commute home, and a fixed daytime dark/sleep period) phase delayed almost as much as expected after two days. Thus, the study is on track to achieve a compromise phase position, whereby the sleepiest time of day falls within the beginning of daytime sleep after a night shift and the end of nighttime sleep on days off. The control group remained in typical dim room light during the night shift, wore sunglasses with lighter lenses during the commute home, and slept whenever they wanted after each night shift. They did not phase shift very much (<1 h), which is typical of real night shift workers in similar conditions. The next installment of this multi-part study will take a "snapshot" after three simulated night shifts and two days off. It is anticipated that the extra night shift with intermittent bright light pulses and extra delayed sleep/dark period will phase delay the peak of sleepiness of the experimental group to the target compromise phase position between 08:30 and 12:00 h.

Recent reports have reiterated the value of combining bright light during the night shift with regular sleep/dark episodes early in the daytime for promoting circadian adaptation to night shift work. When performing three nights of simulated shift work, subjects receiving 6 h of continuous phase delaying bright light pulses and having early fixed daytime sleep periods showed the largest phase delays, with an average

T_{min} displaced into the beginning of the daytime sleep period (Horowitz et al., 2001). In that study, bright light at night alone and a fixed daytime dark/sleep period alone were each associated with smaller phase delays than the combination of treatments. In addition, with only dim room light exposure at night and a regular sleep/dark period occurring before or after three night shifts, phase advances and delays, respectively, were produced (Horowitz et al., 2001; Santhi et al., 2005). However, these phase shifts were very small, ~2 h or less, and were insufficient to produce a physiological adaptation to night work. Consequently, a regular sleep/dark period or nighttime bright light exposure alone is unlikely to be of much utility in facilitating re-entrainment to an abrupt shift of the sleep period, such as that which occurs with night shift work.

In conclusion, the circadian rhythms of our experimental group are phase delaying as expected, with intermittent bright light during the night shift, sunglasses during the commute home, and a fixed dark/sleep period. Future studies will determine whether the compromise phase position can be achieved and maintained with these three interventions while also maintaining baseline levels of sleep, performance, and alertness. If successful, these results could be utilized by permanent night shift workers and their employers.

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