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# Shaping the light/dark pattern for circadian adaptation to night shift work

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ABSTRACT

This is the second in a series of simulated night shift studies designed to achieve and subsequently maintain a compromise circadian phase position between complete entrainment to the daytime sleep period and no phase shift at all. We predict that this compromise will yield improved night shift alertness and daytime sleep, while still permitting adequate late night sleep and daytime wakefulness on days off. Our goal is to delay the dim light melatonin onset (DLMO) from its baseline phase of ~21:00 to our target of ~3:00. Healthy young subjects ($n$=31) underwent three night shifts followed by two days off. Two experimental groups received intermittent bright light pulses during night shifts (total durations of 75 and 120 min per night shift), wore dark sunglasses when outside, slept in dark bedrooms at scheduled times after night shifts and on days off, and received outdoor light exposure upon awakening from sleep. A control group remained in dim room light during night shifts, wore lighter sunglasses, and had unrestricted sleep and outdoor light exposure. After the days off, the DLMO of the experimental groups was ~00:00–1:00, not quite at the target of 3:00, but in a good position to reach the target after subsequent night shifts with bright light. The DLMO of the control group changed little from baseline. Experimental subjects performed better than control subjects during night shifts on a reaction time task. Subsequent studies will reveal whether the target phase is achieved and maintained through more alternations of night shifts and days off.



## 1. Introduction

Night shift work is associated with performance and alertness deficits during night shifts [1–3]. While these decrements reduce worker productivity and in some fields may endanger the individual night shift worker, the potential sequelae for a number of professions extend beyond the worker and the employer, increasing the risk of accidents and injury for society. This risk is exemplified by those in the medical profession, notably medical residents, who often face extended duration (on-call) night shifts. An increase in the frequency of these extended duration shifts has been linked to higher risk of fatigue-related medical errors and preventable adverse events during the work shift, as well as a higher risk for motor vehicle crashes and near misses during the commute home after a night shift [4,5]. Other professions in which night shift alertness is integral to public safety include air traffic controllers [6] and nuclear power plant operators.

The personal health risks of night shift work are well documented. Decreased sleep quantity with subsequent sleepiness and fatigue are prevalent amongst night shift workers [3,7–9]. Night shift work is associated with increased incidence of cardiovascular dysfunction [10,11], gastrointestinal disturbance [9,12], cancer [13–15], and reproductive dysfunction [12,16], as well decrements in psychological well being [17,18]. In addition, social, family, and marital relationships can be disrupted due to night work schedules [19–21].

The circadian clocks of most night shift workers do not phase shift to realign with a night work/day sleep schedule [22]. Performance impairments during night work are largely due to circadian misalignment (i.e., trying to be alert and perform around the circadian peak of sleepiness) combined with an accumulation of homeostatic sleep pressure, which is in itself secondary to sleep deprivation produced by that circadian misalignment. Reducing misalignment between the circadian clock and a daytime sleep period attenuates the nighttime performance/alertness impairments associated with night shift schedules [23].

In laboratory-based studies, scheduled exposure to bright light and darkness is an effective method for reducing or eliminating the circadian misalignment produced by an abrupt shift of the sleep schedule [24–27]. No simulated shiftwork studies have incorporated days off into the protocols, so the efficacy of scheduled exposure to light and darkness to reduce circadian misalignment over longer periods of night work and days off remains to be fully investigated. In a field study of night shift nurses who worked several weeks of night shifts interspersed with days off, a combination of bright light during night shifts and scheduled daytime sleep/dark completely re-entrained most of these subjects by the end of the intervention [28].

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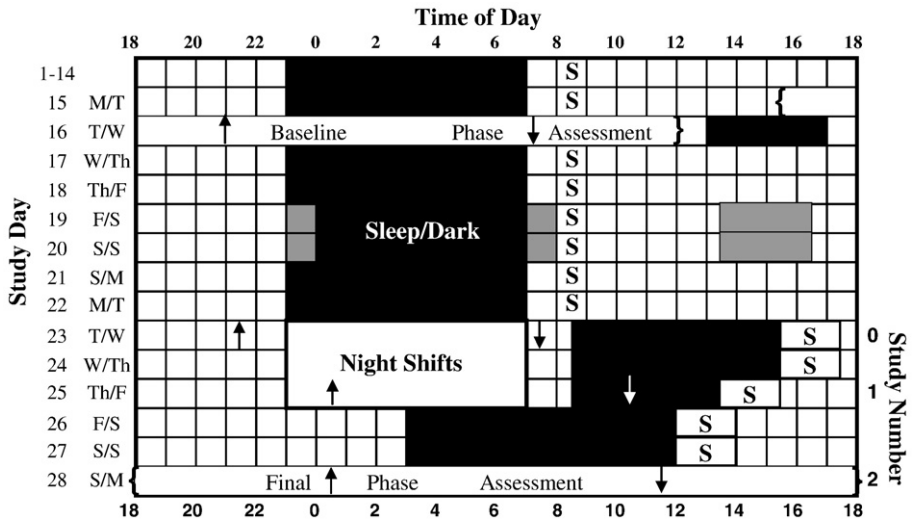


**Fig. 1.** Diagram of the protocol for studies 0, 1, and 2 in the series to test whether scheduled bright light and dark can phase shift the circadian clock to a compromise phase position, and maintain it there despite intervening days off. Study numbers on the right show the days on which each study was ended, and on which a final phase assessment was conducted. The sleep schedule shown during the section with night shifts (from day 23 on) is for the experimental groups only. The control groups were free to sleep at times of their choosing starting after the first night shift. Upward arrows show the dim light melatonin onset (DLMO), downward arrows the offset (DLMOff). For the baseline phase assessment (day 16), these phase markers are averaged for the experimental groups of studies 0, 1, and 2. Also shown is the final position of these phase markers for study 0, which ended and had the final phase assessment on day 23 [33], for the experimental groups of study 1, which ended on day 25 [30], and study 2 (reported here), which ended on day 28. Day 28 depicts the average phase marker position for the two experimental groups of study 2. The pattern of bright light pulses during the night shifts is shown in Fig. 2. On days 1–22 "S" indicates that subjects were required to go outside for at least 15 min of sunlight between 8:00 and 9:00. After day 23, the "S" symbols depict the "light brake" when subjects were required to go outside for at least 15 min within the first 2 h after waking. Subjects wore sunglasses whenever outside in daylight. The lightly shaded boxes on study days 19 and 20 indicate optional weekend sleep, when subjects were permitted to go to bed and awaken 1 h later, and to take naps. This optional sleep was also permitted on the weekends during days 1–14. In the text, study day numbers correspond to the rows shown in the figure, the 24 h from 18:00 to 18:00.

However effective scheduled bright light and darkness are for promoting alignment of the circadian clock to a nocturnal schedule, few permanent night shift workers desire to maintain such a completely shifted sleep schedule on days off [29]. Indeed, despite exposure to zeitgebers that produced re-entrainment to night work and day sleep, most nurses in a field study slept at night (i.e. slept out of phase) on days off [28]. We have thus proposed a compromise in which the sleep schedule for a night worker on days off is later than for typical day workers, but earlier than sleep that occurs after a night shift. We propose using scheduled bright light and darkness to partially delay the circadian clock to reduce misalignment between night work and daytime sleep, but not delay the clock so far as to preclude late nighttime sleep on days off [30–32].

We are testing a schedule with blocks of night shifts interspersed with days off. Subjects are exposed to phase-delaying intermittent bright light during night shifts, scheduled sleep/dark after night shifts and on days off, dark sunglasses to reduce bright light exposure during travel home from night shifts, and an afternoon outdoor light "brake" to keep the circadian clock from delaying too far. This protocol begins with a baseline sleep schedule of 23:00–7:00, which could be as late as 00:00–8:00 on the weekends. After two weeks on this schedule, when a baseline phase assessment occurs, our marker of circadian phase, the dim light melatonin onset (DLMO), occurs at ~21:00 [30,33]. After another 6 days of baseline, the night shift section of the study begins. Daytime sleep after night shifts begins at 8:30 (bedtime is delayed 9.5 h), while bedtime on days off is 3:00. To achieve a compromise circadian phase position, we propose a ~6 h delay of the DLMO, such that the DLMO occurs at ~3:00. The body temperature minimum (Tmin), which coincides with peak subjective sleepiness [34–36], objective sleep propensity [37–39], the circadian nadir in alertness [26,35,40] and the largest decline performance [26,36,37,41], occurs ~7 h after the DLMO [40,42–51]. Thus, with a DLMO ~3:00, the time of peak sleepiness will occur ~10:00, which is during the daytime sleep episode after night shifts as well as during late nighttime sleep on days off.

To test this schedule, we end the study on different subsequent days throughout the protocol and conduct a circadian phase assessment to determine whether the target phase position has been reached or maintained. Here we report results from the second study in the series, with a final phase assessment after three night shifts and two days off.

## 2. Methods and design

Fig. 1 illustrates the first 4 weeks of the protocol used in this series of studies. In this report we describe the results from study 2 (marked by the numbers on the lower right side of the figure). Comprehensive descriptions of the methodology for this series of studies have been described elsewhere: for study 0, which did not include night shifts, but measured circadian phase after two and three weeks of baseline sleep [33], and for study 1, which had two night shifts [30]. The current study (#2) is a between subjects design consisting of a control group and two experimental groups.

### 2.1. Subjects

Forty subjects were enrolled in this study. Eight subjects (4 in experimental group 1, 2 in experimental group 2, and 2 in the control group) withdrew from the study or were dropped for noncompliance, leaving 32 subjects who completed the study. One subject was excluded from analysis due to low melatonin levels. Demographics for the remaining 31 subjects are shown in Table 1. Subjects were free

**Table 1**
Demographics of the three study groups

| Group | *n* | M:F | Age (mean±SD) | M/E[a] (mean±SD) |
|---|---|---|---|---|
| Control | 12 | 4:8 | 23.7±3.6 | 53.1±7.2 |
| Exp 1 | 9 | 3:6 | 28.9±5.8[b] | 55.4±10.8 |
| Exp 2 | 10 | 7:3 | 21.1±2.4 | 51.8±7.5 |

[a] Morningness–Eveningness score [71].
[b] $p<0.05$, experimental group 1 vs control and experimental group 2.