Using Light to Facilitate Circadian Entrainment from Day to Night Flights

Nita Lewis Shattuck; Panagiotis Matsangas; James Reily; Meghan McDonough; Kathleen B. Giles

BACKGROUND: As part of a larger project to provide recommendations regarding limitations and best practices for shifting aviators from day to night operations, a study was conducted to assess the efficacy of high energy visible (HEV) light to shift the circadian rhythm in humans. The study attempted to replicate the patterns of military aviators who could be required to shift abruptly from day to night flight operations.

METHODS: Simulated flight performance and salivary melatonin levels of 10 U.S. military aviators were collected over a 3-night period using a within-subject dim light melatonin onset (DLMO) study design. Data were collected in a laboratory with participants returning home to sleep following each of the three evenings/nights of data collection. Light treatment included a single 4-h exposure of blue-enriched white light (~1000 lux) on night 2. Data collected included melatonin levels, light exposure, sleepiness, cognitive workload, and simulated flight performance.

RESULTS: The average delay in melatonin onset was 1.32 ± 0.37 h (range: 53 min to 1 h 56 min). Sleepiness ($P = 0.044$) and cognitive workload ($P = 0.081$) improved the night following the light treatment compared to the baseline. No systematic differences were identified in flight performance.

DISCUSSION: The HEV light treatment successfully delayed the circadian phase of all participants even though participants' ambient light levels (including daylight) outside the laboratory were not controlled. These findings were used to develop circadian synchronization plans for aviators who are asked to transition from day to night operations. These plans will be assessed in a follow-on study in an operational unit.

KEYWORDS: circadian rhythms, circadian misalignment, high energy visible light, night shiftwork, dim light melatonin onset, simulated flight performance.

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Fatigue and sleep issues continue to appear in aviation mishap reports. A recent Naval Safety Center study found 20% of naval aviation accidents over a 5-yr period were caused in part by fatigue and fatigue-related issues, with an estimated cost of \$842M.[16] Compared to day flights, night flights (i.e., flights beginning at the end of evening twilight to sunrise) are more demanding due to multiple factors, including reduced visibility, a heightened reliance on flight instruments, and the possible requirement for night vision goggles. Additionally, the transition from day flights to night flights is especially challenging due to the need to realign one's circadian rhythm, i.e., the ~24-h rhythm of our internal biological clock that regulates the timing of events such as sleep, alertness, mood, and hormone release at specific times of the biological day.

When crewmembers are not accustomed to working nights, night flights may coincide with aircrew circadian low points, magnifying the already elevated risk levels for night mishaps. This elevated risk is clearly illustrated in a flight mishap that took place in the early morning hours of December 6, 2018, resulting in the deaths of six U.S. Marine Corps aircrew members along with the loss of two aircraft. In the investigation that followed, fatigue was identified as a major contributor to the

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mishap, with the transition from day to night flights specifically called out as a critical source of risk.

Military leaders are frequently confronted with decisions about how best to manage the risks inherent in aviation. The Naval aviation community refers to two documents for managing crew rest and circadian rhythms: Commander Naval Air Forces M-3710.9 and Navy Medicine P-6410.[5,8] The information found in these policies has remained essentially unchanged for several years, without specific guidance on safe transitioning between day and night flights. In response to the 2018 mishap report, the Assistant Commandant of the Marine Corps requested the review and revision of these aviation operations policies to update the guidance for the fleet. Consequently, our research team was asked to study the problem and provide recommendations regarding best practices for shifting aviators from day to night operations. An important operational question was the number of days needed to safely adjust when transitioning from day to night flight operations.

The scientific literature clearly shows that circadian rhythms are responsive to environmental cues called "zeitgebers", a German word that means "time-giver". Zeitgebers can entrain and reset one's internal circadian rhythms to align with their external environment.[7,24] Physical exercise, the timing and composition of meals, and social interactions are known to affect human circadian rhythms.[3,4,25,27,28] However, the dominant and most potent circadian synchronizer is light. When delivered at appropriate times, light can effectively realign the endogenous circadian rhythm. Light can also be an equally powerful circadian disrupter if it is applied inappropriately. Three factors are critical when administering light affecting the circadian system: the timing, the intensity of the light source, and the spectral characteristics of the light. High-energy visible (HEV) light, also known as blue-enriched white light, has spectral characteristics that are most effective at impacting the circadian system.[6]

Several studies using light have assessed the rate of circadian adaptation when shifting the daily schedule from day to night work. Czeisler and colleagues found that an 8-h exposure to high-intensity light (7000–12,000 lx) at night in a laboratory setting can reset the circadian rhythm by ~1.6 h/d.[11] Results from another study, conducted on participants living at home, showed that a 2-h exposure to ~1770–2800 lx of light in the evening was associated with a rate of adaptation of ~2 h/d.[20] Gander and Samel found an average shifting rate of 2 h/d by using a 5-h exposure to >3500 lx of light at night in their laboratory-based study.[22] Dawson and Campbell showed that exposure to bright light in the laboratory (4-h exposure to 6000 lx between 24:00 and 04:00) resulted in an accumulating shift of 5–6 h during the 3-d experiment.[12] In an at-home study, Eastman and Martin[19] demonstrated that a 6-h nighttime exposure to ~5000 lx of light—while also avoiding exposure to light during circadian inappropriate times—resulted in an average phase delay of 2.4 h/d and an average phase advance of 1.6 h/d.[17,19]

Other studies have assessed the effects of light and melatonin combined with shifting the timing of the sleep schedule. For example, advancing the sleep schedule by 1 h/d, combined with intermittent bright light from light boxes (~5000 lx) for the first 3.5 h after waking in the morning and melatonin taken in the afternoon, can phase advance the circadian clock by ~1 h/d.[33] Paul and colleagues evaluated an afternoon regimen of 3 mg slow-release melatonin with and without next morning 1-h exposure to green light treatment (350 lx) for circadian phase advance.[31] Results showed the effect of melatonin in the afternoon (average phase advance of 0.72 h when administered independently of light) and exposure to green light upon awakening (average phase advance of 0.31 h when administered independently of melatonin) was additive, demonstrating that multiple circadian zeitgebers may be more effective than a single one.

In conclusion, the findings presented herein suggest that strategic exposure to bright light can be a valuable tool for aviators to use to entrain their circadian rhythm when transitioning from a day to night schedule. However, several limitations were identified in the studies we reviewed. First, some of these studies used body temperature to assess circadian entrainment,[11,20] not the dim light melatonin onset (DLMO) method that is considered the gold standard for assessing circadian phase.[29] Second, applying results of these studies to operational settings in which naval aviators work must be considered carefully. In typical naval aviation units, aviators may be assigned to a regular daily flight schedule, but their work may also involve other assigned duties outside of flying. Consequently, they may be exposed to light at times that are outside the ideal windows for entraining to a night flight schedule. Many of the studies we reviewed were conducted in controlled light conditions.[20,22] Also, the duration of the light treatment in these studies would not fit into the daily schedule of aviators, whereas exposure to high intensity light has been associated with eye strain and migraine headaches.[21,36] Given these limitations, our study was specifically designed and conducted to determine the efficacy of HEV light exposure for circadian entrainment in conditions similar to the operational environment that aviators experience.

METHODS

Subjects

A total of 10 individuals volunteered to participate in the study. All participants were qualified aviators from their respective U.S. military communities (Army, Air Force, Marine Corps, and Navy). Participants had varying amounts of flight experience representing diverse platforms. After a preliminary examination of the data, one male participant was excluded from further analysis due to abnormally high salivary melatonin levels throughout both the day and night. Therefore, the analysis was based on nine participants (eight men and one woman, 30 to 44 yr of age, total flight hours = 1282 ± 689). The Naval Postgraduate School Institutional Review Board approved the study protocol and all participants provided written informed consent.

Equipment and Materials

The enrollment questionnaire consisted of a demographic section, items assessing flight experience, use of prescribed or over-the-counter medication, and whether the participant had ever been diagnosed with a sleep-related disorder. In the flight sessions, participants completed the Epworth Sleepiness Scale (ESS) to assess average daytime sleepiness and the Karolinska Sleepiness Scale (KSS) to assess individual situational momentary sleepiness.[1,23] A modified version of the Bedford Workload Scale (BWS) was used to assess cognitive workload.[34]

Sleep patterns were assessed by wrist-worn activity monitors (Spectrum Plus; Philips-Respironics; Bend, OR, USA) augmented with self-reported activity logs, validated methods to collect objective sleep data in field studies.[2] Actigraphic data were collected in 1-min epochs and scored using Actiware software version 6.0.0 (Phillips Respironics). The medium sensitivity threshold (40 counts per epoch) was used, with 10 min of immobility as the criterion for sleep onset and sleep end. All values are the default for this software.

HOBO pendant data loggers were used to assess participants' exposure to ambient light when not in the laboratory. Participants were instructed to wear the device outside their clothing on their upper arm for the duration of the study (approximately 10 d) while awake. Circadian-targeted lighting was administered in the laboratory using light boxes (Circadian Positioning Systems, Inc., Newport, RI, USA). These light boxes were set to a blue boosted bright light setting for the light treatment (~1000 lx) and a dim light setting at all other times (<10 lx). The light boxes were approximately 3–6 ft away from the participant. The position of the light boxes was such that the participants did not look directly at the light. Before each night session, light levels were verified using a CL-500A illuminance spectrophotometer (Konica Minolta, New Jersey, USA). Saliva samples were collected using salivettes (Sarstedt, Nümbrecht, Germany). The samples were centrifuged and chilled immediately and stored at −20°C within 7 h of collection, in accordance with standard practices.[10]

Flight performance was assessed using two identical flight simulator systems which included the X-plane 11 flight simulator software by Laminar Research (Columbia, SC, USA) installed on a desktop computer paired with a yoke/pedal/throttle-lever control interface. The simulated aircraft was a Cessna 152 with analog gauges. Participants performed three ~20-min flight scenarios (A, B, C) of increasing difficulty. Each scenario started in the vicinity of the final approach course 20 mi away from the runway. Participants were instructed to fly the plane using the pretuned instrument landing system to maintain course and descent rate. Flight performance was assessed by three variables: airspeed, horizontal deflection, and vertical deflection. Participants were instructed to fly the plane by maintaining 60 kn as their indicated airspeed. Participants assessed their horizontal and vertical deflection using the course deviation and glideslope indicator. The indicator is designed to give a relative measurement over the width of the localizer beam. The full horizontal deflection of the course deviation and glideslope indicator is 2.5°. Negative numbers indicate horizontal positioning left of the center of the radio beam, whereas positive numbers indicate positioning to the right. In terms of their vertical position, participants were instructed to stay at the vertical center of the localizer beam.

Procedure

The 10-d longitudinal within-subject DLMO study was conducted in hybrid conditions. The main experiment was conducted in controlled conditions in the Human Systems Integration Lab, but participants returned home to sleep following each of the three evenings/nights of data collection.

Participants were recruited by a one-time mass email and a study flyer posted on the Naval Postgraduate School student muster page for 2 mo. As shown in **Fig. 1**, the 10-d study was divided into a 7-d sleep/wake control period and a 3-d laboratory data collection period. On the first day of the sleep/wake control period, volunteers completed the enrollment questionnaire and were issued an activity monitor, an activity log, and a light sensor to wear throughout the study. Participants were instructed to maintain their habitual sleep patterns. Actigraphic data were used to determine participants' habitual bedtimes for scheduling their night sessions and to ensure that participants were maintaining a consistent schedule for bedtime and awakening the week prior to the laboratory data collection.

On Day 6, participants conducted a familiarization data collection session that included all three flight scenarios in the simulator. They returned to the lab on the morning of Day 8 for their first laboratory data collection session ("Morning"), completed the preflight questionnaire to assess their state before the commencement of the data collection, and performed the three flight scenarios (A, B, and C, in that order) in simulated daytime settings. The entire lab was illuminated at normal office lighting conditions during this period. After each scenario, the participants provided a saliva sample and completed the KSS and BWS.

Participants returned to the lab 3 h prior to their habitual bedtime in the evening of Day 8 ("Night 1"), Day 9 ("Night 2"), and Day 10 ("Night 3") for their three nighttime data collection sessions. Participants were instructed to have a light meal before their night session and to avoid caffeinated beverages and nicotine for 4 h before arrival. Two separate areas of the Human Systems Integration Lab, a light-controlled area and a flight simulator area, were used for data collection. Upon arriving at the lab, participants stayed in the light-controlled area for the period before the flight tests. Ambient light in the light-controlled area was dim (dim red-enriched light settings of less than 10 lx) on Nights 1 and 3 and bright on Night 2 with lighting provided by the Circadian Positioning Systems light boxes. Specifically, lights during Night 2 were set at a blue-enriched white light setting of approximately 1000 lx (measured at eye level using a spectrophotometer) for the first 4 h following arrival at the lab. After the 4-h exposure to bright light, participants were moved to the flight simulator area and given 30 min in dim light (less than 10 lx) to allow them to dark adapt before performing the three night flights.

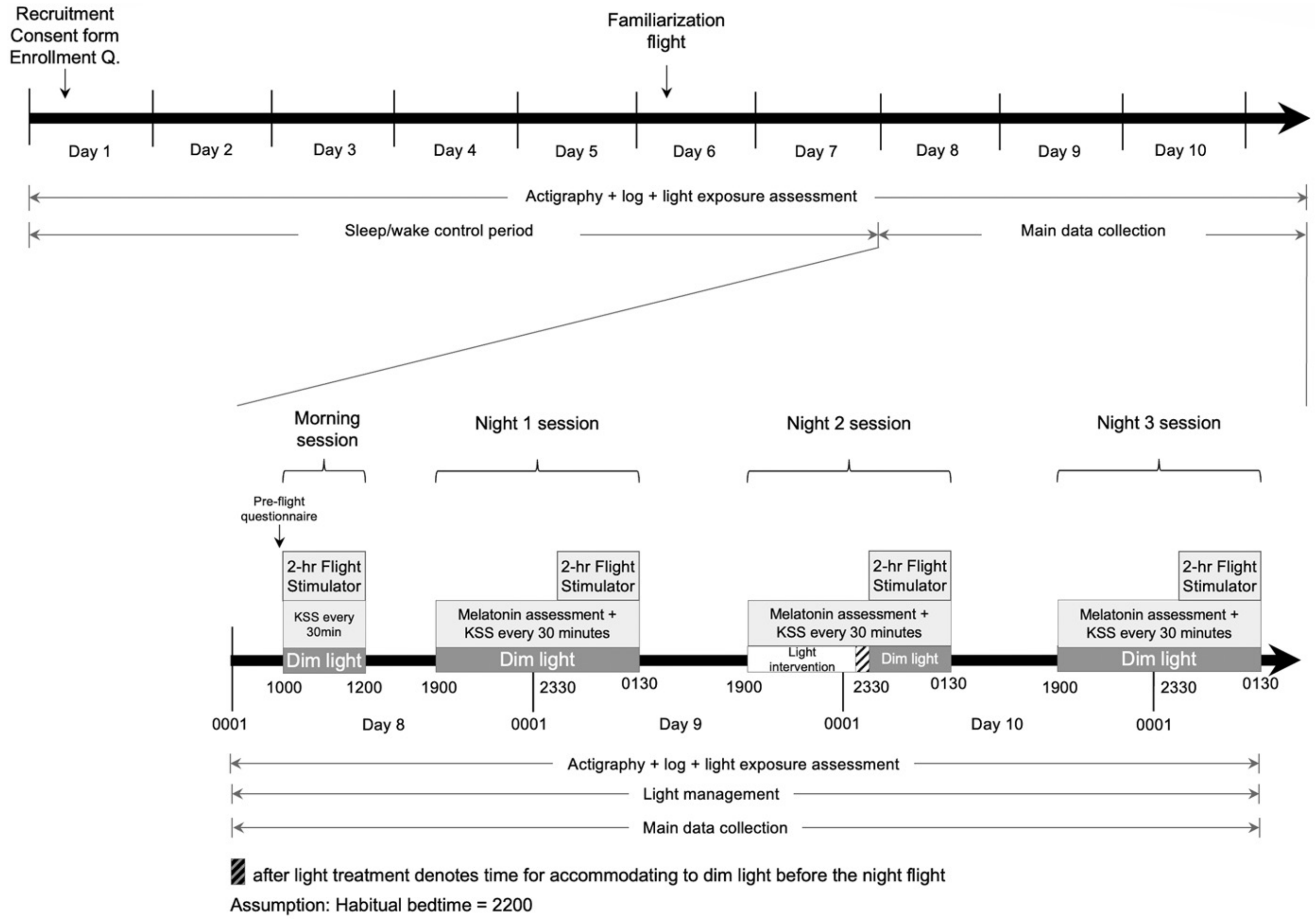

Fig. 1. Overview of the experimental protocol. The diagram describes a protocol tailored for a habitual bedtime of 22:00.

Upon arrival for the night sessions, researchers verified that the participants were in good health, had maintained a regular sleep schedule, and had refrained from caffeine or nicotine products for at least 4 h before arriving at the lab. For the first 4 h of each night session, participants were isolated in the light-controlled area, where they were allowed to work on homework, read, watch movies, use the internet, etc. On Nights 1 and 3, all personal electronic devices were kept on the lowest brightness to ensure dim light conditions were maintained.

Each participant completed the KSS and provided a saliva sample every 30 min during each of the three nighttime sessions, for a total of 12 samples per night. The first salivary melatonin sample was collected 2.5 h before their habitual bedtime and the last sample was collected 3 h after habitual bedtime. After each flight, participants completed the KSS and the BWS, and provided a saliva sample. The light levels were measured during each saliva collection using a spectrophotometer. After each data collection session, participants returned home just as they would at the end of a night flight.

The only difference between Night 2 and Nights 1 and 3 was the light treatment, i.e., the bright (~1000 lx) light exposure for the first 4 h when participants were in the light-controlled area. On Night 2, eight salivary samples were collected in bright light conditions while the four final samples (when participants were performing the flight scenarios) were collected in dim light conditions (<10 lx). The timing of the data collections was such that participants were in the bright light setting (~1000 lx) for 3 h before and 1 h after their habitual bedtime. In each data collection session, participants spent approximately 6.5 h in the lab.

Statistical Analysis

Salivary melatonin levels were assessed by the SolidPhase Laboratory, Portland, ME, USA. Melatonin concentration in saliva was determined using radioimmunoassay (Alpco, Salem, NH, USA) with a sensitivity of 0.9 $\text{pg} \cdot \text{mL}^{-1}$, intra-assay coefficient of variation of 7.9%, and interassay coefficient of variation of 9.8%. A 4 $\text{pg} \cdot \text{mL}^{-1}$ threshold was used to determine the DLMO through linear interpolation.[9] Circadian phase shifts were calculated by contrasting the DLMO of Night 3 (post-treatment) with Night 1 (baseline). Imputation was applied to seven (1.75%) missing KSS values based on the average of the adjacent values of the participant with the missing data.

Flight performance was assessed by the mean and standard error of three variables, i.e., airspeed deviation from 60 kn, horizontal deflection, and vertical deflection. For each flight, these metrics were aggregated between two points, i.e., at the point at which the participants passed the final approach fix until they were 300 ft above the runway. The Federal Aviation

Administration's definition of a final approach is the flight path from the final approach fix, a specific distance from the airport designated on a map, to the runway. Measurements from 300 ft above the runway to landing were excluded because participants had the runway in sight and were using outside visual cues to land.

We conducted a descriptive analysis of participants' demographic characteristics, participant state at the beginning of the main data collection period, and the change in DLMO to assess circadian entrainment. Exposure to ambient light was determined by visual inspection of exposure patterns in the sleep/wake control and the main data collection periods. Next, we used mixed-effects model analysis to assess differences in KSS and BWS scores between data collections, with a fixed effect of data collection session (Night 1, Night 2, Night 3) and data collection order, and a random effect of subject. Post hoc comparisons were based on Dunnett's test with control accounting for multiple comparisons. Also, mixed-effects analysis was used to assess differences in flight performance between the night data collection sessions. Fixed effects included data collection session (Night 1, Night 2, Night 3), flight profile (A, B, C), and the interactions between data collection session and flight profile, whereas the random effect was the subject. Post hoc comparisons were based on the Tukey honest significant difference (HSD) test, accounting for multiple comparisons.

Statistical analysis was conducted with JMP statistical software (JMP Pro 16; SAS Institute; Cary, NC, USA). Data normality was assessed with the Shapiro-Wilk W test. An alpha level of 0.10 was used to determine statistical significance. The decision to use this alpha level was based on the small number of participants in the study. Summary data are reported as mean ± SD.

RESULTS

As verified by actigraphy, habitual bedtimes ranged from 21:30 to 00:00. The average ESS score was 4.40 ± 1.78 at the beginning of the day data collection session, with all participants having normal daytime sleepiness (ESS score ≤10).

Visual inspection of the light exposure outside the laboratory showed that participants were exposed to ambient light mainly during the morning and early afternoon hours. In general, this pattern was consistent during both the sleep/wake control period of the experiment and the main data collection period. These findings suggest that, when not in the lab, participants were exposed to light at times that are known to counteract the expected phase delay from the light treatment on Night 2. **Fig. 2** shows light exposure for each participant, averaged by hour of day. Participant 9 wore his/her HOBO light logger only during the sleep/wake control period. Average daylight conditions are denoted by the white background.

The DLMO analysis showed that the light treatment on Night 2 successfully delayed the circadian phase of all participants on Night 3. Specifically, the average phase delay was 1.32 ± 0.37 h, ranging from 53 min to 1 h 56 min.

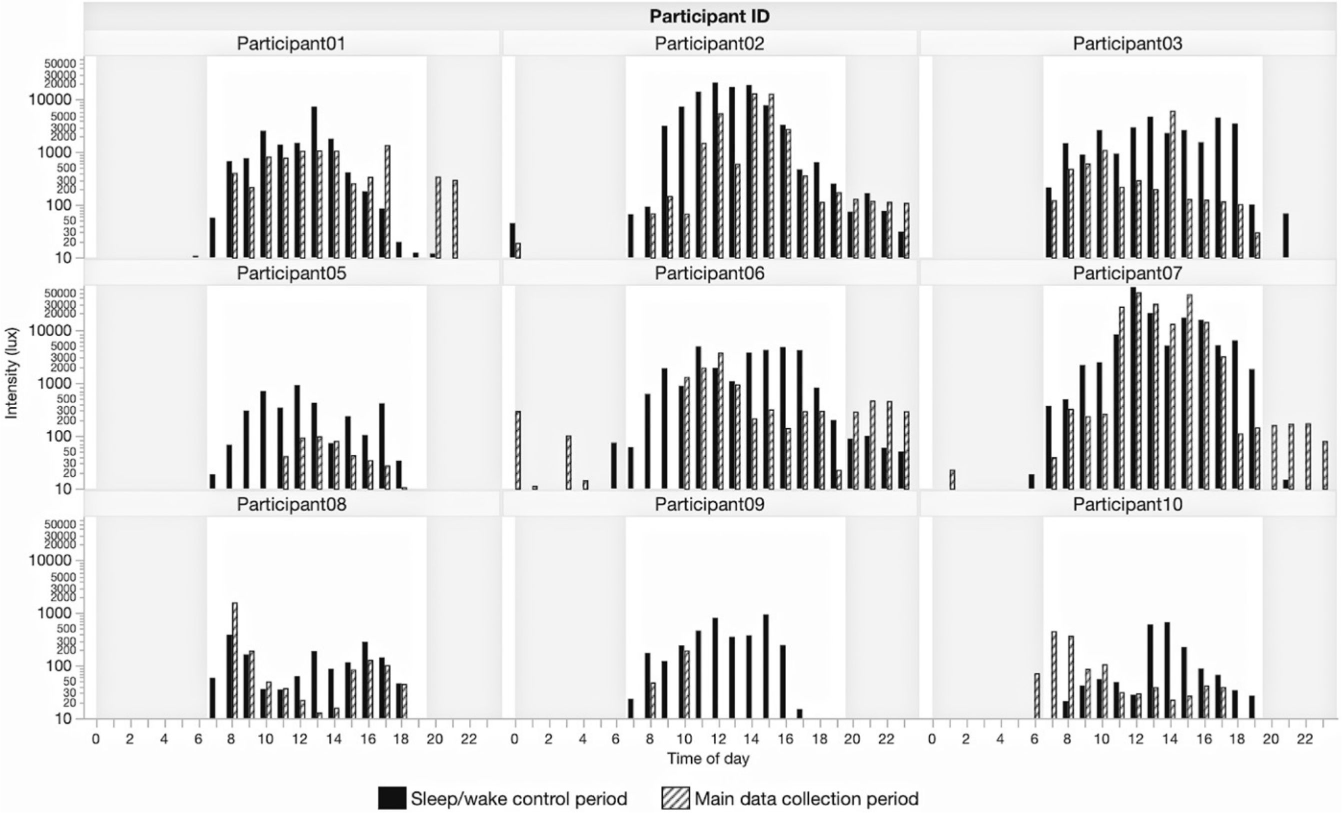

Fig. 2. Average light exposure by hour of the day and experimental period for each participant. The white backgrounds denote average daylight conditions.

Mixed-effects model analysis showed that sleepiness, as assessed by KSS scores, increased consistently over the course of each of the three nighttime data collection sessions ($P < 0.001$) and the scores differed between nights ($P = 0.006$). Post hoc analysis showed that KSS scores in Night 3 (post-treatment) were lower (better) than Night 1 (Dunnet's test with control, $P = 0.044$) and equivalent to Night 2 (Dunnet's test with control, $P = 0.607$). These results suggest that reported sleepiness was lower (i.e., participants were more alert) the night following the light treatment compared to the baseline.

Mixed-effects model analysis showed that subjective workload, as assessed by BWS scores, increased consistently over the course of each of the three nights ($P < 0.001$), and the scores differed among nights ($P = 0.001$). Post hoc analysis showed that BWS scores on Night 3 (post-treatment) were lower (better) than on Night 1 (Dunnet's test with control, $P = 0.081$), and equivalent to Night 2 (Dunnet's test with control, $P = 0.120$). These results suggest that self-reported cognitive workload was lower the night following the light treatment compared to the baseline.

Fig. 3 shows the KSS and BWS scores for all data collection sessions. The morning session was not included in the statistical analysis; however, the corresponding data are included in the diagrams for completeness. The KSS trends are based on a spline smoother with lambda = 1.81. The BWS trends are based on a spline smoother with lambda = 3.24.

Mixed-effects analysis showed that the standard error of airspeed differed between data collection sessions ($P = 0.035$). Specifically, the airspeed on Night 3 (mean = 1.33 knots, SE = 0.180) was better (less) than on Night 1 (mean = 1.82 knots,

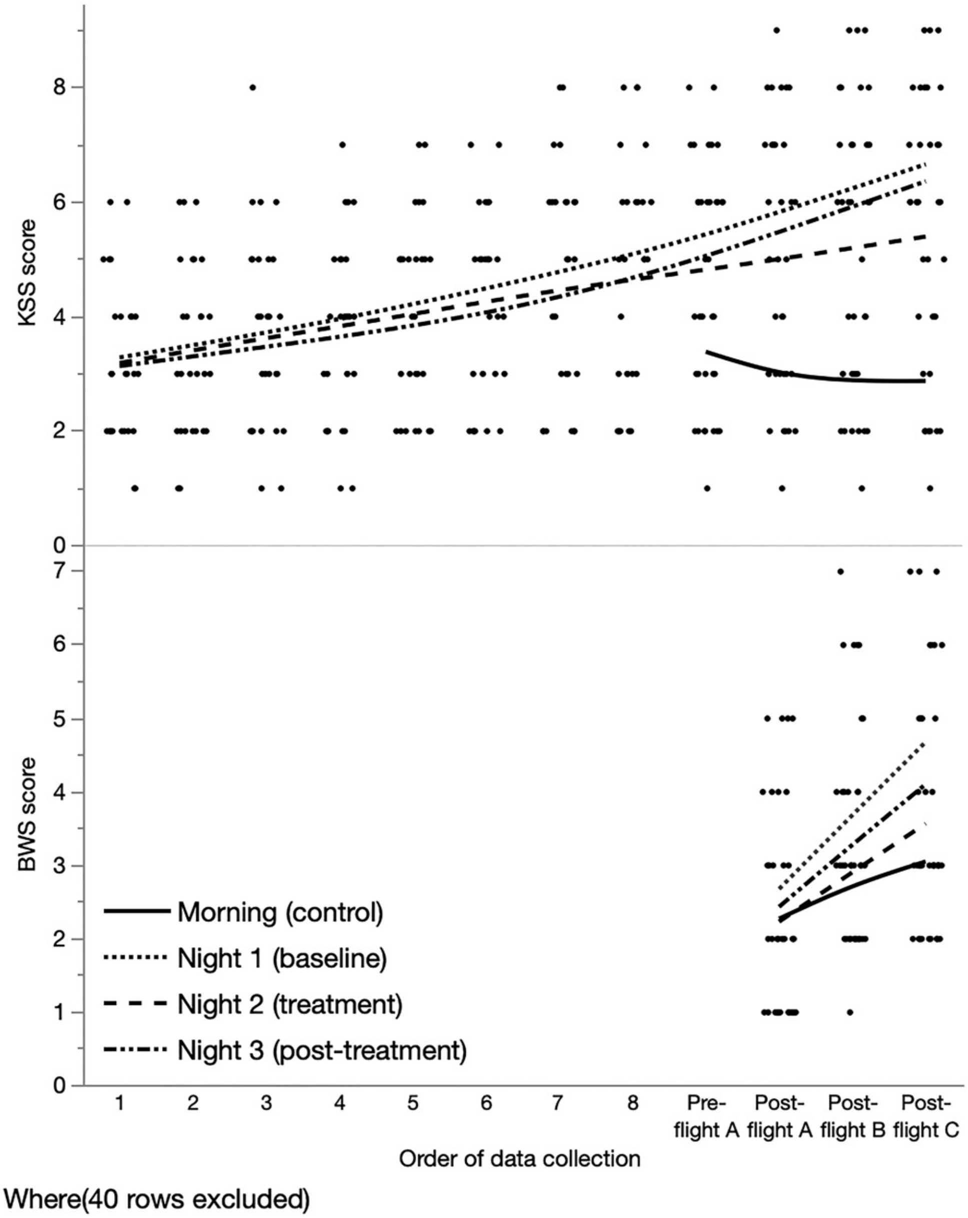

Fig. 3. KSS and BWS scores. Individual participant data (markers) and group trends (lines) are shown.

SE = 0.178; Tukey HSD test, $P = 0.027$). All other results were not statistically significant (Tukey HSD test, all $P > 0.25$).

DISCUSSION

We conducted a study to assess the efficacy of bright light exposure for phase-delaying the circadian clock when individuals transition from working days to a night regimen. Our results showed that a single 4-h exposure to the blue-boosted light setting of approximately 1000 lx successfully entrained (i.e., delayed) the circadian phase of all participants an average of 1.32 ± 0.37 h (ranging from 53 min to 1 h 56 min). The importance of this finding becomes clear if we consider that our participants were also exposed to some sunlight throughout the day, partially counteracting the entraining effect of the light exposure in the lab. Theoretically, the magnitude of the phase delay that could be achieved by the light treatment could be increased if aviators adopt and abide by a strict light management protocol throughout the day. Also, the phase delay could be increased further if a battery of carefully aligned synchronization methods could be used, including shifting the daily work/rest schedule and chronobiotics (e.g., melatonin, caffeine).[30,32]

From a behavioral and light-exposure perspective, the study protocol replicated, to the extent possible, the work/rest patterns of aviators in operational environments when they are working in daylight conditions and are required to shift to night flight operations. Also, the light treatment in the lab (1000 lx) was conservative compared to light levels used in other studies. This decision was based on our intention to increase the external validity of our results by using parameters that could realistically be used in military and other operational settings. Producing extreme bright light intensities requires specialized equipment, which may be challenging to implement in operational settings due to the increased logistical footprint and the associated costs. Also, exposure to high intensity light can lead to adverse health outcomes, e.g., eye strain and migraines.[21,36] Thus, the results presented here demonstrate that, even when implemented in a manner that is realistic and not ideal (i.e., without strict adherence to light management and without maximizing light intensities), bright light treatment is a valuable tool to aid aviators when transitioning from day to night operations.

Two more issues should be discussed in relation to our findings. First, with the data collected in our study, we cannot quantifiably distinguish the effect of the light treatment per se from the effect of the delayed sleep schedule resulting from the late evening data collection sessions in the laboratory. Results from earlier studies, however, suggest that changes in the sleep-wake cycle provide relatively minimal drive for resetting the human circadian pacemaker.[15] Consequently, we expect that the phase delay identified in our study can be attributed predominantly to the light treatment.

The second issue is that we did not identify any systematic changes in flight performance. This (non) finding may be explained by our participants' flight proficiency and experience levels and the characteristics of the simulated flights. Our participants were all highly qualified military aviators who were asked to fly a single-engine aircraft for a relatively short period of time in controlled laboratory conditions. Their expertise and flight experience may have masked any potentially deleterious effects of fatigue as well as any positive effects of the light treatment in the simulated flights. Also, the largest effects of fatigue on performance are expected with extended time-on-task,[14,26] but our aviators were required to perform for a short amount of time (three 20-min flight scenarios). Enrolling only inexperienced aviators, increasing the task difficulty, and/or simulating longer flights may have revealed an effect of the light treatment on performance.

The primary goal of this project was to provide recommendations regarding best practices for shifting aviators from day to night operations by facilitating circadian realignment, thereby mitigating pilot fatigue. Based on the findings of our study, combined with relevant scientific evidence from other authors[18,30] and existing military regulations,[5,8,13,35] we developed recommendations that fell into two categories. The first category includes general recommendations for fatigue management, including operational scheduling, sleep hygiene training and education, sleep environment, timing of sleep and naps, light management in the operational environment, use of chronobiotics (e.g., melatonin and caffeine), nutrition, and exercise. The second category of recommendations includes two notional plans for consideration. One plan is designed for aviators transitioning from day to night operations by gradually shifting their schedule, while the second plan is designed for aviators who are unable to gradually transition between schedules due to an abrupt and/or unexpected schedule change.

The study has several caveats. First, we had a small sample of aviators. Second, laboratory conditions cannot replicate the operational environment. To ameliorate this limitation, we used a hybrid study design in which we collected data both in and outside of the laboratory. Participants were allowed to leave the lab at night, return home to sleep, and continue their normal daily activities. This approach increased the external validity of our findings while ensuring adherence to the light intervention in the laboratory. Conducting the study in an operational environment, however, will yield the most valid results. Also, we could not impose any type of crew coordination or radio communication scenarios due to the limitations of the commercial off-the-self simulator we used. Future efforts should revise the flight scenarios to become more challenging and realistic. All the study participants had somewhat consistent sleep schedules before the commencement of the main data collection in the lab. These schedules certainly differ from sleep schedules in operational settings, which may be inconsistent, demanding, and highly stressful. Lastly, we were not able to have a control group due to the limited pool of aviators available to participate in our study, which occurred at the height of the COVID-19 pandemic before vaccines were available. A control group would have allowed us to separate the phase delay effect of the light treatment from the effect of sleeping later due to the experimental protocol.

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