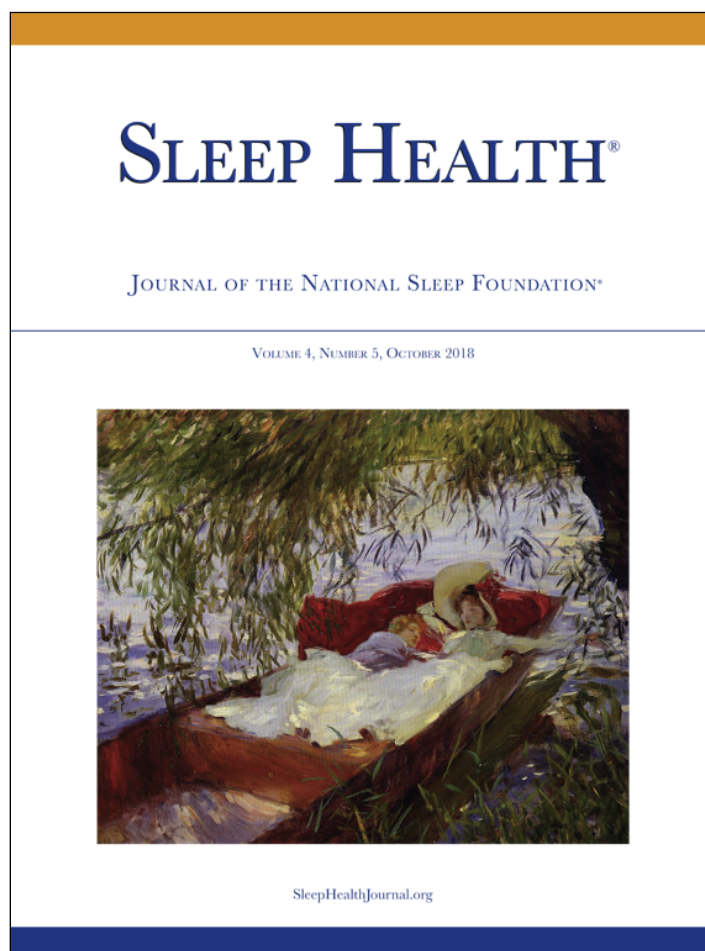


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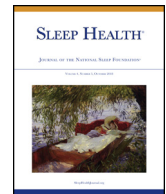
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Sleep and neurobehavioral performance vary by work start time during non-traditional day shifts

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ABSTRACT

Introduction: It is established that shiftwork causes sleep loss and circadian misalignment. Individuals who work non-traditional day shifts that encroach into typical sleep times, such as those in the service and transportation sectors, may also experience sleep and circadian disruption. We aimed to determine how neurobehavioral performance and sleep would be affected by work start time among individuals working a non-traditional daytime shift pattern.

Methods: We collected sleep diaries, wrist-worn actigraphy (CamNtech, Cambridge UK), and the psychomotor vigilance task (PVT) from 44 pilots (4F) who worked a shift rotation consisting of a five-day baseline block starting in the mid-morning (baseline), five early shifts (early), five high workload midday shifts (midday), and five days of late shifts (late), each separated by 3–4 days off.

Results: Mixed-model analysis revealed that individuals obtained less sleep when working the early shifts (5.70 ± 0.73 h) relative to baseline (6.78 ± 0.86 h; $P < .01$). Sleep duration declined significantly from the beginning to the end of late shifts ($P = .003$). All shifts were associated with decreased reaction time on the PVT relative to baseline (236 ± 48 ; early, 257 ± 70 ms; midday 261 ± 62 ms; late 266 ± 64 ms; $P < .01$ for all).

Conclusions: We found that non-traditional day shifts encroach on an individual's sleep opportunity and such shifts could be a contributing factor to the high prevalence of sleep deficiency observed in modern society. Our findings suggest that it would be prudent for industries requiring such shifts to expand fatigue risk management training to individuals classified as day shift workers.

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Introduction

Sleep loss and circadian misalignment experienced by shiftworkers have been implicated in numerous incidents and accidents.^{1,2} Much of the research effort to date has focused on understanding and mitigating the negative effects of sleep loss and circadian misalignment during rotating shift work, night work, extended duty work shifts, and jet lag.^{3,4} However, many occupations, such as those in the service and transportation industries, require that workers engage in non-traditional daytime work, with variable daily start and end times, often requiring high workload. Early starts and late finishes may not be classified as night work in

these occupations, due to the majority of work hours occurring during the day (e.g. a 5:00 AM to 2:00 PM shift or a 2:00 PM to 11:00 PM shift), but such shifts have the capacity to cause circadian disruption and may be a factor in the high prevalence of sleep deficiency among the general population.^{5,6}

Performance impairment due to sleep loss and circadian misalignment among airline pilots is of particular concern, due to the safety implications to passengers and crew alike. There are many factors in daytime short-haul aviation operations that have the potential to cause sleep deprivation and disruption of the circadian rhythm, including irregular schedules, early report times,^{7,8} and late finishes.⁹ In addition, short haul operations typically involve higher workload in the form of frequent takeoffs and landings, which exposes the crew to an increased opportunity for error relative to long-haul operations.^{10,11} Sleep loss and circadian desynchrony of this nature is associated with degradation in alertness and performance.¹²

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These concerns have been addressed by regulating agencies in the United States and Europe through limitations on the number of hours that a crewmember can work based on the work start time and the number of flight segments scheduled (FAA 14 CFR 117; Commission Regulation (EU) 83/2014), however, it is unclear how schedule design within the legal limits impacts sleep and alertness in an operational environment, particularly when work shifts are scheduled during the day. To this end, we conducted a study of short-haul commercial airline operations using a controlled shift design in an effort to better understand how work start time and workload affect sleep duration and timing, alertness, cognitive performance, and circadian phase.

Participants and methods

Participants

All pilots working for a single airline, at one of the airline's largest hubs, were eligible for participation. There were no other exclusion criteria, as we wanted to characterize sleep, performance, and circadian phase under real world conditions. Study participants were invited to participate in the study via an e-mail distributed through the Fatigue Risk Management group at the airline. Participation in the study was voluntary and all study participants provided written informed consent prior to engaging in any study procedures. The

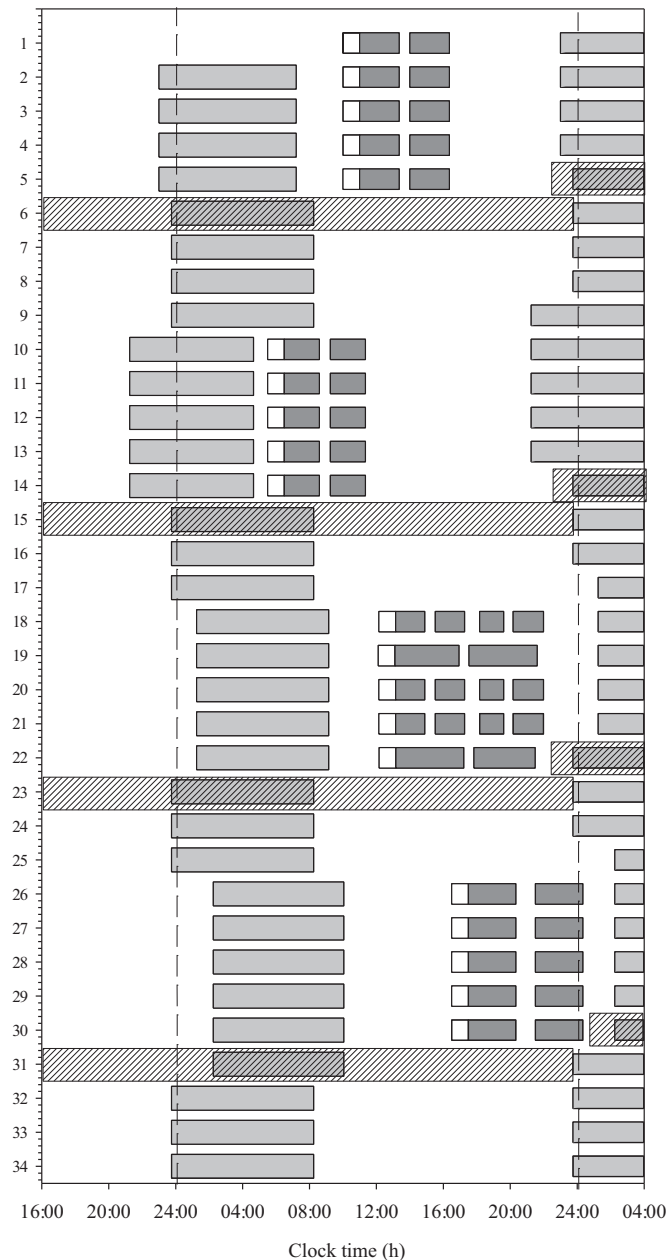


Fig. 1. Study protocol raster plot. Each row represents one day of the study. The x-axis is plotted over 36 hours to show work schedule and available time for sleep on the same line. Flight duty schedule (dark gray) and sleep periods (light gray bars) are shown including the pre-flight report time (open bar) with breaks between flights. Baseline duties are on days 1–5, early report duties on days 10–14, midday duties on days 18–22 and late reports on days 26–30. Shaded hatched bars indicate the scheduled time of the post-block urine collection.

study was approved by the Human Research Institutional Review Board at NASA Ames Research Center (protocol number HRI-319).

Study protocol

All the pilots in this study flew a fixed schedule (Fig. 1). The schedule consisted of a cycle where the pilots worked a baseline block (baseline) with five days of short work shifts, typically starting in the mid-morning, with two flight segments lasting approximately two hours each. This was followed by four days off, five early starts (early) followed by three days off, five midday starts (midday) that on average included more flight segments and longer work shifts, followed by three days off and then five late duties (late), scheduled to start in the late afternoon followed by four days off. Given the need to maintain airline operations, there were variations in the roster among the participants; however, pilots were asked to avoid trading shifts in order to preserve the study schedule. By design, each participating pilot returned to his or her home base at the end of every work day during this study. Sleep timing and activities during non-work time were unrestricted.

Each participant was provided an iPod, pre-loaded with the study questionnaires, daily sleep diary and study schedule and an iPod version of the psychomotor vigilance task (PVT) developed at NASA Ames Research Center. The participants completed the sleep diary every morning within 30 minutes of waking and every evening within 30 minutes of going to bed. The morning sleep diary also included the Samn Perelli fatigue scale and a sleep quality rating.¹³ As is the case for all handheld devices, touch events from the iPod included a latency of $\sim 68 \pm 30$ ms relative to traditional PVT boxes and provide faster response times relative to push-button response boxes.¹⁴ We removed this system latency prior to analysis. Each participant was oriented to the proper procedure for completing the PVT and completed a training session in the presence of a study staff member.

Participants wore an actiwatch (CamNtech, Cambridge, UK) throughout the entire study period. On rest days, they were asked to complete the PVT three times every day; 1–2 hours after waking, 8–9 hours after waking and 1–2 hours before sleeping. On work days, they were asked to complete the PVT upon waking, before bed, at the top of descent on every sector, and post flight.

Urine collection

All study participants were invited to participate in an optional sub-study involving 24-hour urine collection for the assessment of 6-sulphatoxymelatonin (aMT6s). Volunteers were asked to collect urine samples during a 24-hour period on non-work days immediately following each study block. Participants collected all urine produced in 24-hours over four-hour blocks during the day and eight hours during the night. At the end of each urine collection block, participants were asked to record the clock times of each void and the sample time. They measured and recorded the total volume produced using collection urinals marked by milliliters, sampled a 5–10 ml aliquot and recorded the sample number of the tube used. Participants were asked to return the samples to study personnel within three days, where they were processed and shipped to the vendor for assay.

Actigraphy analysis

Actigraphy data were analyzed using Actiware Software (Phillips-Respironics, Bend OR) to determine sleep latency, sleep duration, wake after sleep onset (WASO) and sleep efficiency.

6-sulphatoxymelatonin assay

Urinary aMT6s concentrations were measured by radioimmunoassay by Stockgrand, Ltd., University of Surrey (Guildford, UK), using the methods of Aldhous and Arendt.¹⁵

Rhythm analysis

6-sulphatoxymelatonin values in ng/mL were converted to ng/h and subjected to best-fit cosine analysis (SAS software, version 9.2 Cary, NC) to analyze the patterns of the 24-hour urine collection. A cosine transformation was applied to the time variable using 24 hours as the default circadian cycle, and the PROC NLIN procedure in SAS was used to estimate the acrophase (peak time, circadian nadir) of the aMT6s rhythm. Results were used in the present analysis if they showed a significant cosine fit at the $P < .05$ level.

Statistical methods

All analyses were calculated using SAS Software (Cary, NC). Univariate summary statistics were calculated for all variables of interest by work shift block.

In order to account for the within-subjects study design, we evaluated all condition effects for sleep and performance outcomes using repeated measures analysis of variance (proc mixed in SAS), with unstructured covariances, using participant as a repeated factor. In order to evaluate whether sleep and performance outcomes varied by day on a given schedule, we applied linear mixed effects models to the changes in sleep and performance by day. In order to account for individual differences in adaptation to a given schedule, we allowed the intercept and slope to vary by individual. Finally, we compared the slope of the change in sleep and PVT performance over time by schedule type (baseline, early, midday, late) using an analysis of response profiles. The baseline data collection period was considered baseline for all analyses.

Results

Forty-four pilots (4 female) aged 30.8 ± 7.1 years (mean \pm SD) volunteered for the study. The study work schedule varied as designed (Table 1). The baseline characteristics of the study participants are presented in Table 2.

Impact of schedule start time on sleep

Sleep metrics were obtained through sleep diaries and actigraphy. Subjective sleep timing, disruption and duration obtained from the sleep diary differed by schedule type (two participants were excluded from all sleep diary analyses due to non-compliance with the sleep log). Study participants attempted to initiate sleep at significantly different times during each of the study blocks relative to their baseline bedtime (Table 3, baseline v. early starts $P < .0001$, v. midday starts $P < .0001$, v. late starts $P < .0001$). This difference ranged from attempting sleep approximately two hours earlier during the early

Table 1
Characteristics of work days

	n (work days)	Start time (mean h; SD)	Number of flight sectors (mean n; SD)	Flight duration (mean h; SD)
Baseline	167	10:17 (3:50)	2.01 (0.15)	2.36 (0.73)
Early	196	05:24 (0:38)	2.01 (0.07)	2.09 (0.52)
Midday	171	13:52 (1:20)	2.82 (0.98)	2.47 (1.12)
Late	176	16:33 (1:33)	2.01 (0.21)	2.83 (1.47)

SD = standard deviation; h = hour.

Table 2
Demographic characteristics of study participants

n	44
Age	30.8 (± 7.1)
Height (cm)	179.6 (± 5.8)
Weight (kg)	78.0 (± 10.2)
BMI (kg/m ²)	24.15 (± 2.6)
Self-reported sleep need (h)	7.9 (± 0.7)
Commute time (m)	40 (± 22)
MEQ score	51.4 (± 7.1)
	n (%)
Female	4 (9)
Marital Status	
Single	30 (68)
Married	14 (32)
Current smokers	2 (5)

cm = centimeters; kg = kilograms; BMI = body mass index; kg/m² = kilograms per meter squared; h = hours; m = minutes; MEQ = morningness-eveningness score.

starts block to attempting to sleep just over three hours later than baseline during the late start block. Study participants attempted to go to sleep approximately 30 minutes later on rest days compared to baseline days ($P < .01$). Wake time also differed by work shift, with the participants waking three hours earlier than baseline on early shifts (Table 3; $P < .0001$), nearly two hours later on midday shifts ($P < .001$), two and a half hours later on late shifts ($P < .0001$), and approximately one hour later on rest days ($P = .001$). These changes in sleep timing resulted in a self-reported loss of sleep on the early ($P < .001$) shifts (Table 3). Participants rated their fatigue upon waking as higher on early shifts according to the Samn Perelli scale, but did not rate sleep quality as different from baseline on any of the shifts (Table 3).

As expected, study participants overestimated sleep duration compared to actigraphy-derived sleep measures (Table 4). Actigraphy-derived sleep latency was not significantly different for any work schedule type or rest days relative to baseline (early $P = .36$, midday $P = .66$, late $P = .17$; Table 4). Sleep efficiency was not significantly different for any work schedule type relative to baseline (early $P = .34$, midday $P = .55$, late $P = .12$). Wake after sleep onset (WASO) was not significant for midday ($P = .12$) or late work shifts ($P = .71$) relative to baseline; however, there was significantly more WASO during the sleep preceding early work shifts compared to baseline ($P = .03$). Actigraphy-derived total sleep time did not differ between baseline and midday or late work shifts, but was significantly shorter during early work shifts ($P < .001$).

In order to determine whether each work shift schedule type resulted in a change in sleep outcomes over time on that schedule, we evaluated the change in total sleep time (TST), sleep latency, sleep efficiency and WASO from the night before a work shift block to the night preceding the last shift in the sequence. For this mixed-model analysis we allowed the slopes and intercepts to vary by individual in order to account for inter-individual differences in response to different schedule types.

There was no significant change in any sleep outcome by day on the baseline schedule (sleep duration, $P = .76$; latency, $P = .33$; efficiency, $P = .45$; and WASO, $P = .71$). On the early work shift rotation, sleep latency declined significantly from the beginning to the end of the early

shifts ($P < .03$), while sleep efficiency improved by day on the early shift rotation ($P = .03$). There was no significant change by day in nightly sleep duration ($P = .81$) or WASO ($P = .19$) on the early work shift rotation. During the midday schedule, sleep duration ($P = .22$) and sleep latency ($P = .55$) did not vary by day of work shift. WASO declined significantly by day ($P = .04$), which resulted in improved sleep efficiency by day on that schedule ($P = .04$). During late work shifts, sleep duration declined significantly from the first day to the last day on that block ($P = .003$). WASO also decreased by each day of the block ($P = .03$). Sleep latency ($P = .19$) and sleep efficiency ($P = .99$) did not change significantly by day of late work shift.

Impact of schedule start time on performance

The psychomotor vigilance task was completed 3140 valid times by participants during the study. Four participants were excluded from all PVT analysis due to having insufficient or outlier data. We observed a statistically significant increase in mean reaction time (RT) and lapses (> 500 milliseconds), and a decrease in transformed reaction time (response speed; *rspeed*, 1/RT) between the baseline condition and each of the more challenging flight schedules (Table 5; early, RT $P = .003$; *rspeed* $P = .003$, lapses $P = .005$; midday, RT $P = .002$, *rspeed* $P = .003$, lapses $P = .02$; late, RT $P = .0006$, *rspeed* $P = .0005$, lapses $P = .009$). On rest days, reaction time, response speed, and lapses did not differ significantly from the baseline condition (RT $P = .14$; *rspeed* $P = .17$; lapses $P = .18$).

In order to determine whether each work schedule type resulted in a change in PVT outcomes over time on that schedule, we evaluated the change by day on each schedule. For this analysis we allowed the slopes and intercepts to vary by individual in order to account for inter-individual differences in response to different schedule types. In mixed model analyses, we found that mean reaction time ($P = .45$), lapses ($P = .62$), and response speed ($P = .17$) did not vary by day on the baseline schedule.

During the early and late schedules, PVT reaction time and lapses increased significantly from the beginning to the end of each rotation, while response speed decreased (early, RT $P < .0001$, lapses $P = .0003$, *rspeed* $P < .0001$; late, RT $P = .004$, lapses $P = .0008$, *rspeed* $P < .0001$ Fig. 2). On the midday schedule, only response speed varied by day on that schedule (midday, RT $P = .33$, lapses $P = .39$, *rspeed* $P = .03$).

We next conducted an analysis of response profiles comparing the change in slope for reaction time, lapses, and response speed by work shift day to the slope of the baseline schedule. We found that the slope was significantly different for the early starts (RT $P = .008$; lapses $P = .02$; *rspeed* $P = .001$; Fig. 2) and late finishes (RT $P = .0005$; lapses $P = .01$; *rspeed* $P = .006$) compared with the baseline schedule. For the midday schedule, only the slope of response speed was different by day compared to baseline (RT $P = .26$; lapses $P = .64$; *rspeed* $P = .02$).

Impact of schedule start time on circadian phase

Thirteen participants volunteered to collect urine samples after each work shift block for assessment of 6-sulfatoxymelatonin

Table 3
Sleep diary-derived sleep outcomes by schedule type

	n	Bedtime (h, SD)	Wake time (h, SD)	Sleep Duration (h, SD)	Samn Perelli AM (SD)	Sleep Quality (SD)
Baseline (ref.)	39	23:10 (1:41)	7:20 (1:49)	8.2 (0.9)	3.3 (1.1)	2.4 (0.7)
Early	42	21:14 (1:01)**	4:29 (0:47)	7.4 (0.9)**	3.8 (1.0)**	2.5 (0.6)
Midday	41	01:19 (0:43)**	9:11 (0:58)	7.9 (1.1)	3.3 (1.0)	2.3 (0.6)
Late	40	02:18 (1:07)**	9:57 (1:11)	7.8 (1.4)*	3.5 (1.0)	2.3 (0.7)
Rest days	42	23:47 (0:50)**	8:16 (0:58)	8.5 (0.9)*	3.1 (0.7)	2.4 (0.5)

* $P < .05$, ** $P < .01$; h = hour, SD = standard deviation, Samn Perelli AM refers to a self-report fatigue rating that was taken within 15 minutes of waking in the morning.

Table 4
Actigraphy-derived sleep outcomes by schedule type (from night before first shift to night before last shift)

	n (study participants)	Total Sleep Time (h, SD)	Sleep Latency (m, SD)	Sleep Efficiency (% , SD)	Wake After Sleep Onset (m, SD)
Baseline (ref)	37	6.78 (0.86)	18 (22)	83 (7)	54 (37)
Early	41	5.70 (0.73)**	21 (17)	81 (7)	45 (30)*
Midday	41	6.83 (1.00)	16 (17)	83 (7)	53 (31)
Late	39	6.69 (0.93)	24 (28)	81 (9)	55 (40)
Rest days	42	6.82 (0.90)	19 (13)	80 (7)	62 (35)

* $P < .05$, ** $P < .01$ Rest day sleep outcomes include only the first three days following each duty block. Rest day sleep outcomes are shown for reference, but are not included in the mixed model analysis.

(aMT6s), a reliable marker of circadian phase.¹⁶ The mean circadian phase varied as expected with work shift start time (Fig. 3). In mixed model analysis, the mean circadian phase shifted significantly earlier on the early starts relative to baseline ($P = .004$), but midday and late shifts were not different from baseline ($P = .67$ and $P = .30$, respectively). The mean circadian phase shift was significantly later for the midday shifts compared to the early shifts ($P = .02$). The mean circadian phase shift between the midday and late schedules did not differ significantly ($P = .19$).

There were wide inter-individual differences in baseline circadian phase. The aMT6s acrophases following the baseline condition ranged from one participant who had an early 02:04 (CI: 01:35–02:44; $P < .001$) baseline phase to another participant who had a baseline phase that occurred 4.5 hours later at 06:33 (CI: 5:59–7:08; $P < .001$; Fig. 3). The range in circadian phase between individuals after the early starts block ranged from an early phase of 24:30 (CI: 23:20–25:41; $P < .01$) to a late phase of 04:52 (CI: 04:13–05:30, $P < .001$). The change in phase from the baseline block to the early starts block ranged from a phase advance of 5:44 h to a phase delay of 1:14 h, with nine participants experiencing a phase advance and two participants experiencing a phase delay.

The range in circadian phase between individuals following the midday starts ranged from an early phase of 23:59 (CI: 21:43–26:14; $P = .01$) to a late phase of 5:53 (CI: 5:06–6:46; $P < .001$). The change in phase from the early starts to the midday starts ranged from a 1:33 h advance to a 5:05 h delay, with one participant experiencing a phase advance and seven participants experiencing a phase delay. The range in circadian phase following the late starts ranged from an early phase of 01:57 (CI: 24:59–02:56; $P < .001$) to a late phase of 06:25 (CI: 5:29–7:20; $P < .01$). All participants who completed urine collection during late starts experienced a phase delay, ranging from 0:28 h to 2:58 h. The change in phase for individuals from the beginning to the end of the study ranged from a 3:34 h phase advance to a 2:11 h phase delay.

Discussion

Our study represents the first systematic evaluation of sleep, performance and circadian phase by shift type among short-haul pilots. Although directly reflecting the findings for short haul pilots, the changes that we found in sleep and performance are likely generalizable across many industries that require workers to engage in non-

traditional daytime work. Our study confirms that sleep duration and reaction time are affected by schedule type even when work start times are scheduled to occur during the day. We found that pilots obtained less sleep and exhibited slower reaction time on early schedules compared to baseline. We further found that early and late starts elicited a progressive decline in sleep duration and a deterioration of reaction times by day on that schedule type. We also found evidence of degraded performance during midday starts in the absence of sleep loss relative to baseline, suggesting that increased workload may also contribute to performance impairment. When we examined circadian phase shifts in a subset of participants, we found wide inter-individual differences in both baseline phase and the magnitude and direction of phase shift in response to different work shift schedules. Although these findings are consistent with circadian phase shifts observed in laboratory studies,¹⁷ our data confirm that such differences exist among an operationally critical population, i.e. short-haul commercial airline pilots. Our findings raise the concern that work shift schedules that do not violate regulated limits may still yield performance decrements among individuals required to work such schedules.

Few other studies have examined the impact of schedule design on short-haul airline operations. In a self-report survey of 739 pilots, those on short-haul work shifts indicated that the three biggest factors associated with fatigue were flying more than four segments, consecutive early starts, and night work shifts.¹¹ Our study provides objective confirmation that these factors contribute to performance impairment. We observed reductions in sleep duration and timing on the early and late work shift blocks, which coincided with increased reaction time and lapses on the PVT. Although we did not observe a significant reduction in actigraphy-derived sleep duration on the midday starts compared to the baseline work shifts, we did observe significant impairment in PVT performance relative to baseline, suggesting that increased number of segments leads to decreases in performance even in the absence of a difference in sleep outcomes. The participants in our study averaged less than seven hours of sleep during the study, even on rest days. Although this is consistent with the amount of sleep obtained by ~30% of the general population,¹⁸ it is understood that this amount of sleep is insufficient for optimal alertness and performance.^{19,20} It is possible that pilots were able to overcome chronic partial sleep loss through strategic use of countermeasures to enhance performance during work shift schedules that included few flight segments (i.e. during the baseline

Table 5
PVT outcomes by schedule type

	n (participants)	Mean Reaction Time (ms, SD)	Response Speed (SD)	Mean Lapses > 500 ms (SD)
Baseline (ref.)	38	236 (48)	4.84 (0.61)	3.1 (4.1)
Early	40	257 (70)**	4.63 (0.66)**	4.4 (5.4)**
Midday	39	261 (62)**	4.56 (0.66)**	4.7 (5.1)*
Late	38	266 (64)**	4.51 (0.63)**	4.7 (5.0)**
Rest days	40	249 (56)	4.69 (0.62)	4.0 (4.5)

* $P < .05$, ** $P < .01$; SD = standard deviation, ms = milliseconds.

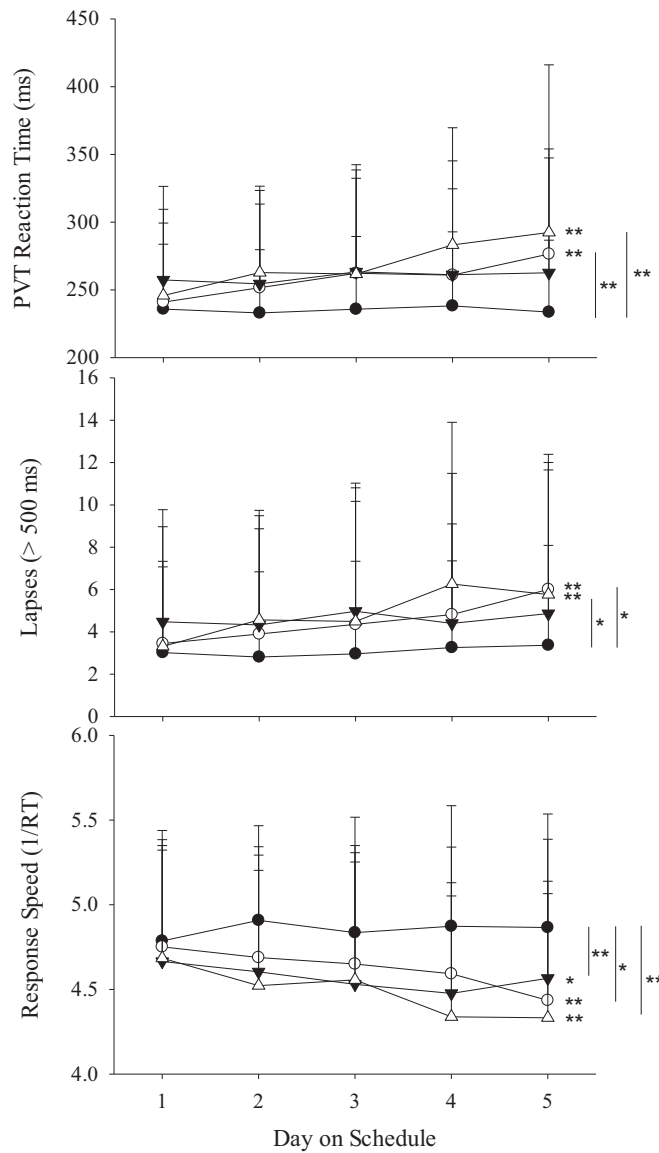


Fig. 2. PVT reaction time (RT, top panel), lapses >500 ms (middle panel), and response speed (bottom panel) by day on each schedule. Significance for linear change by day on each schedule is shown as * $P < .05$, ** $P < .01$, differences in slope relative to baseline are indicated by vertical bars; ms = milliseconds. Baseline = filled circles, early = open circles, midday = filled triangles, late = open triangles.

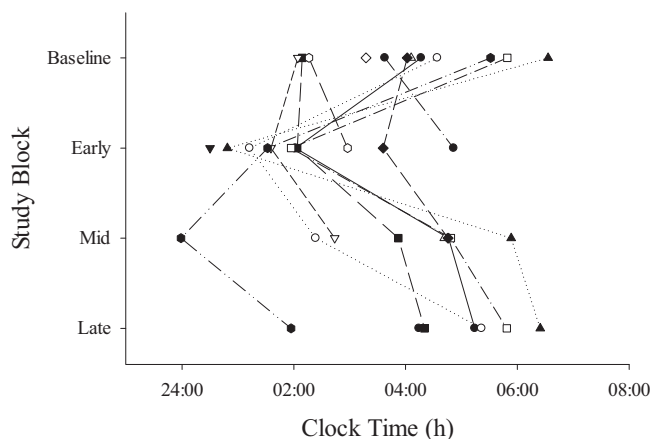


Fig. 3. 6-sulfatoxymelatonin (aMT6s) acrophase, indicating the timing of the circadian nadir by individual and study block.

block), but that additional work shift time arising from multiple flight segments revealed the underlying vulnerability to chronic sleep loss, leading to degraded performance on the midday shifts.

We observed reduced sleep quality and quantity on early starts that remained reduced low for the duration of the early work shifts. We also found that neurobehavioral performance was reduced, with progressive degradation in reaction time by day on the early schedule. Early starts require earlier bedtimes relative to later morning starts for most people. We found that the pilots in this study attempted to go to bed earlier than normal in advance of an early start. Although they attempted to sleep earlier, they obtained less sleep, reported feeling unrested, and had poorer performance on the early starts relative to both the baseline work shift schedule. This is consistent with findings from other studies in pilots^{8,11} and others.²¹

Prior studies support the notion that early starts have the potential to disrupt sleep and performance. In our study, the pilots attempted to sleep an average of two hours earlier on nights preceding early work shifts compared to baseline, but had to wake three

hours earlier than baseline. Such shortened sleep episodes have been shown to lead to daytime performance impairment.^{19,20} In addition, sleep stage and sleep fragmentation are apparently different on early start schedules, likely due to the truncation of sleep.⁷ Although we did not measure sleep stage, our finding that actigraphy-derived sleep duration on early starts was reduced to 5.70 hours, and that pilots woke three hours earlier on days with early starts, is strikingly similar to the findings of Kecklund and colleagues who measured electroencephalography (EEG) in cabin crew and found that sleep was reduced to 5.33 hours and that crew woke three hours earlier on early starts.⁷ In that study the investigators found no differences in sleep latency, sleep fragmentation or number of awakenings per hour compared to baseline, but they did find that the early starts resulted in a reduction of stage 2 and REM sleep, which may explain why pilots report feeling unrested during early starts. In another study, early starts were associated with elevated cortisol levels that persisted throughout the waking day.⁸ These findings suggest that early starts may be associated with stress response upon waking, which may contribute to poorer subjective ratings of mood and fatigue.

Another factor leading to performance impairment on early starts relates to the individual's circadian phase at the time of sleep initiation. The wake maintenance zone occurs in the hours immediately preceding one's habitual bedtime.²² The wake maintenance zone represents the time of day when the circadian system is promoting the strongest drive to be awake. Abrupt advance shifts in sleep timing have been shown to lead to longer sleep latencies and more sleep disruption in controlled laboratory studies.²³ Consistent with the findings of other studies in operational environments,^{7,24} we did not find that the mean sleep latency was longer on the early starts condition overall, but we did find that sleep latency shortened by day on the early work schedule. This implies that the wake maintenance zone may have inhibited the participants' ability to sleep when starting the early schedule, but over time they may have experienced a circadian phase shift that allowed for faster sleep initiation earlier in the evening. This is consistent with our finding that a majority of the participants who collected urine samples experienced a circadian phase shift to an earlier hour relative to baseline.

Although we found that early starts were associated with short sleep duration and poorer performance, circadian adaptation to early starts is possible with precise control of light and darkness.²⁵ The circadian phase shifting response to light follows a phase response curve (PRC), such that light timed in the relative morning (after the circadian nadir) leads to an advance phase shift and light timed in the relative evening (before the circadian nadir) leads to a delay phase shift.^{26,27} In order to use light as a countermeasure to facilitate circadian phase shifting, it is necessary to determine an individual's circadian phase, so that light may be timed appropriately. Although we did find that the majority of participants who participated in the circadian phase assessment obtained a mean advance, this was not the case for two participants. In our study, the early starts required the pilots to begin work shifts as early as 4:23 AM. Given that the average commute time among participants in our cohort was 40 minutes, early starts required some participants to get up before 3:00 AM in order to allow time for personal hygiene routines, eating and commuting. Three participants had a circadian acrophase of their aMT6s rhythm estimated to be before 3:00 AM at the end of the baseline block, and if these phase estimates are representative of the larger cohort, it would not be surprising that some individuals would experience a circadian phase shift to an earlier, rather than later time. This is particularly concerning, because it implies that the circadian nadir, which is associated with poorest performance and greatest sleep drive,²⁸ may have coincided with work shift start time for some participants. Although we have circadian phase data for only a subset of our participants, we found that sleep duration

remained low and performance declined significantly by day on the early shifts, suggesting that complete adaptation to early starts may not have occurred for some participants. In practice, our results suggest that tailored fatigue risk management programs in industries where non-traditional daytime schedules are required may benefit from providing guidance to workers on how to strategically use light and other countermeasures in order to shift circadian phase prior to early starts.

Late shifts were also associated with poorer sleep and performance outcomes relative to baseline. Unlike early starts, where participants spent an hour less in bed, during late work shifts, the pilots shifted both their bedtimes and wake times approximately three hours later relative to baseline, but spent approximately 30 minutes less time in bed. This modest reduction in time in bed resulted in the significantly shorter duration of sleep obtained by day, as sleep latency, WASO and sleep efficiency were not different from baseline. All participants who completed the urine collection during the late schedule experienced a phase delay. Although our small sample size in circadian phase analysis in this block reduces the generalizability of our results, these findings are consistent with what would be expected given the human phase response curve (PRC) to light.²⁶ During the late work shift block, the timing of the light signal would be expected to precede the circadian nadir given that the mean bedtime following late work shifts was 2:19 AM, and as a consequence of being at work, all participants who participated in the melatonin collection would have been exposed to light on the phase delay portion of the PRC.

Although we were only able to collect circadian phase data in a subset of participants, our circadian phase analysis reveals that individual circadian phase is distributed across a 4.5–6 hour range of time depending on work shift type. In addition, these data demonstrate that the magnitude and direction of phase shifting differs by individual and by work start time. Such findings have been reported in other industries,^{29–32} and in laboratory studies.¹⁷ Circadian adaptation to new sleep–wake schedules is determined by the PRC to light. It can take several days for the circadian system to adapt to a change in sleep wake timing. When individuals are not exposed to light of appropriate intensity, wavelength, and duration, it is possible that adaptation will not occur at all.³³ In addition, when individuals attempt to sleep in a circadian misaligned state, they can experience symptoms of insomnia, further reducing sleep duration.³⁴ Based on the range of circadian phase changes that we observed in the subset of individuals who collected urine samples, it is possible that many individuals remained circadian misaligned during the early and late rotations. The negative consequences of work coinciding with the circadian nadir have been characterized in many cohorts of night shift workers, where the worst performance occurs in conjunction with the circadian nadir, even when an individual obtained sleep prior to the night shift.³³ In our study, participants did not work any shifts that would be classified as night shifts; however, their early start schedules likely required them to be awake during a vulnerable period when the circadian drive to sleep would be high. Although the circadian misalignment that the early work schedules conferred might be considered modest, because the early starts allowed participants to sleep during the biological night, the intersection of some work schedules with the circadian nadir would be expected to confer significant performance impairment.³³

Although we were able to collect a large quantity of data during flight operations, our study is not without limitation. We studied a fixed schedule and did not randomize shift rotations. It is possible that the sleep debt accrued during the early starts block contributed to the reduced performance that we observed in the midday and late blocks. Given that we conducted this experiment within the setting of a busy international airline, there is inherently some misclassification in the work shift blocks. The range of work start times for

baseline included some early starts and the late starts contained some starts earlier than anticipated due to operational requirements. We believe that such error was distributed randomly throughout the study and as a result would attenuate our findings. Although we were only able to collect circadian phase information for 13 participants, our findings are consistent with what has been reported in laboratory and field studies. In addition, there are currently no data to demonstrate how PVT performance relates to operational performance, however, another study has shown that operational errors made by pilots are nearly 50% greater during the hours of 0:00 and 5:59.³⁵ These findings are consistent with our observation that early and late starts were associated with the worst PVT performance, shortest sleep duration and the timing of the circadian nadir for the subset of study participants who collected urine samples for melatonin analysis. As this was a field study, participants may have used countermeasures, such as caffeine during the study, but we do not have enough information about caffeine to determine its potential impact on our findings. We also did not ask about use of alcohol or other substances, which could have affected our findings. It is also important to note that we only evaluated one possible schedule rotation and other schedule designs may yield different performance and sleep outcomes.

Millions of individuals in a variety of occupations are required to work non-traditional day shifts that begin early in the morning or end late at night.³⁶ The changes that we observed in the PVT reveal a potential vulnerability associated with such shifts. There were no accidents or incidents reported during our study; however, our findings may be viewed as revealing one layer of risk that may be manageable in many circumstances, but that could contribute to operational failure when combined with other risk factors, such as poor weather or equipment failure.³⁷ Night and rotating shift work have been associated with increased risk of a myriad of negative health outcomes.³⁸ At the present time, it is unclear whether more modest phase changes exhibit long-term consequences, but recent evidence suggests that variable sleep patterns lead to increased allostatic load.³⁹ Although it may be possible for some industries to modify work shifts to better accommodate workers, it is unrealistic for such shifts to be eliminated completely, particularly in commercial aviation. Our findings suggest that it would be prudent for companies to evaluate the impact of early and late day shifts on sleep and performance to develop schedules that minimize worker fatigue and maximize sleep. It is likely that schedules requiring irregular starts (i.e. work start times that vary by many hours day-to-day) would be associated with poorer performance and reduced sleep duration compared to the controlled schedule that we evaluated due to the difficulty that workers would likely have falling asleep and waking up arising from caused by modest circadian misalignment. On controlled schedules, such as the one we evaluated, targeted strategies and countermeasures could be provided to workers to help individuals better adapt to these types of work shifts. Fatigue risk management programs are currently in place at many airlines and, while the focus of these programs is often on long-haul operations that include jet lag, such programs could be quickly modified to provide support and guidance to airline employees working non-traditional daytime schedules. More research is needed to evaluate whether such education could improve worker sleep and performance on such shifts. If such interventions are shown to be successful, similar fatigue risk management programs could be adopted by other organizations to help workers in other industries cope with non-traditional day shifts.

In summary, we demonstrate that sleep duration was over one hour shorter during early work shifts compared to baseline, resulting in a progressive decline in PVT performance by day on that schedule. Similarly, we observed that late work shifts were associated with a progressive decline in sleep duration by day of the work shift block.

We found evidence of performance degradation on the late shift rotation relative to baseline that progressively declined by day. We also found that midday work shifts, which included higher workload with many flight sectors, was associated with performance impairment in comparison to baseline, but no difference in sleep duration. Our study highlights the wide individual differences in circadian phase and phase shifting among individuals who work non-traditional daytime schedules. These data suggest that some individuals may have more difficulty coping with certain schedule designs even during work classified as a day shift. Such information requires further study to determine whether schedules and countermeasure strategies could be optimized for individuals working such shifts. Our findings highlight the importance of educating individuals working irregular non-traditional daytime schedules on how to use countermeasures to facilitate shifts in sleep timing and on how to protect time to allow for adequate sleep.

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Conflicts of interest

EEF is a consultant for Baby Sleep Science, and has previously consulted with Brigham and Women's Hospital. She has also received travel funding from the University of Chicago and Washington State University. KBG is a consultant for the San Francisco Bar Pilots, and for the National Safety Council. The other authors report no conflict of interest with this work.

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References

- Marcus JH, Rosekind MR. Fatigue in transportation: NTSB investigations and safety recommendations. *Inj Prev*. 2016;23:232–238.
- Mitler MM, Carskadon MA, Czeisler CA, Dement WC, Dinges DF, Graeber RC. Catastrophes, sleep, and public policy: consensus report. *Sleep*. 1988;11(1):100–109.
- Gander PH, Signal TL, van den Berg MJ, Mulrine HM, Jay SM, Jim Mangie C. In-flight sleep, pilot fatigue and psychomotor vigilance task performance on ultra-long range versus long range flights. *J Sleep Res*. 2013;22(6):697–706.
- Eriksen CA, Akerstedt T, Nilsson JP. Fatigue in trans-Atlantic airline operations: diaries and actigraphy for two- vs. three-pilot crews. *Aviat Space Environ Med*. 2006;77(6):605–612.
- Liu Y, Wheaton AG, Chapman DP, Cunningham TJ, Lu H, Croft JB. Prevalence of healthy sleep duration among adults—United States, 2014. *MMWR Morb Mortal Wkly Rep*. 2016;65(6):137–141.
- Liu Y, Croft JB, Wheaton AG, Perry GS, Chapman DP, Strine TW, et al. Association between perceived insufficient sleep, frequent mental distress, obesity and chronic diseases among US adults, 2009 behavioral risk factor surveillance system. *BMC Public Health*. 2013;13:84.
- Kecklund G, Akerstedt T, Lowden A. Morning work: effects of early rising on sleep and alertness. *Sleep*. 1997;20(3):215–223.
- Bostock S, Steptoe A. Influences of early shift work on the diurnal cortisol rhythm, mood and sleep: within-subject variation in male airline pilots. *Psychoneuroendocrinology*. 2013;38(4):533–541.
- Vejvoda M, Elmenhorst EM, Pennig S, Plath G, Maass H, Tritschler K, et al. Significance of time awake for predicting pilots' fatigue on short-haul flights: implications for flight duty time regulations. *J Sleep Res*. 2014;23(5):564–567.

10. Honn KA, Satterfield BC, McCauley P, Caldwell JL, Van Dongen HP. Fatiguing effect of multiple take-offs and landings in regional airline operations. *Accid Anal Prev*. 2016;86:199–208.
11. Bourgeois-Bougrine S, Carbon P, Gounelle C, Mollard R, Coblenz A. Perceived fatigue for short- and long-haul flights: a survey of 739 airline pilots. *Aviat Space Environ Med*. 2003;74(10):1072–1077.
12. Mollicone DJ, Van Dongen HP, Rogers NL, Banks S, Dinges DF. Time of day effects on neurobehavioral performance during chronic sleep restriction. *Aviat Space Environ Med*. 2010;81(8):735–744.
13. Samn S, Perelli L. Estimating Aircrew Fatigue: A Technique with Application to Air-lift Operations. San Antonio, TX: Brooks Air Force Base; 1982 [Contract No.: SAM-TR-82-21].
14. Arsintescu L, Mulligan JB, Flynn-Evans EE. Evaluation of a psychomotor vigilance task for touch screen devices. *Hum Factors*. 2017;59(4):661–670.
15. Aldhous ME, Arendt J. Radioimmunoassay for 6-sulphatoxymelatonin in urine using an iodinated tracer. *Ann Clin Biochem*. 1988;25(Pt 3):298–303.
16. Bojkowski CJ, Arendt J, Shih MC, Markey SP. Melatonin secretion in humans assessed by measuring its metabolite, 6-sulfatoxymelatonin. *Clin Chem*. 1987;33(8):1343–1348.
17. Wright Jr KP, Hughes RJ, Kronauer RE, Dijk DJ, Czeisler CA. Intrinsic near-24-h pacemaker period determines limits of circadian entrainment to a weak synchronizer in humans. *Proc Natl Acad Sci U S A*. 2001;98(24):14027–14032.
18. Schoenborn CA, Adams PE. Health behaviors of adults: United States, 2005–2007. *Vital Health Stat 10*. 2010(245):1–132.
19. Van Dongen HP, Maislin G, Mullington JM, Dinges DF. The cumulative cost of additional wakefulness: dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. *Sleep*. 2003;26(2):117–126.
20. Belenky G, Wesensten NJ, Thorne DR, Thomas ML, Sing HC, Redmond DP, et al. Patterns of performance degradation and restoration during sleep restriction and subsequent recovery: a sleep dose-response study. *J Sleep Res*. 2003;12(1):1–12.
21. Kecklund G, Akerstedt T. Effects of timing of shifts on sleepiness and sleep duration. *J Sleep Res*. 1995;4(S2):47–50.
22. Lavie P. Ultrashort sleep-waking schedule. III. 'Gates' and 'forbidden zones' for sleep. *Electroencephalogr Clin Neurophysiol*. 1986;63(5):414–425.
23. Dijk DJ, Duffy JF, Silva EJ, Shanahan TL, Boivin DB, Czeisler CA. Amplitude reduction and phase shifts of melatonin, cortisol and other circadian rhythms after a gradual advance of sleep and light exposure in humans. *PLoS One*. 2012;7(2):e30037.
24. Gander PH, Gregory KB, Graeber RC, Connell LJ, Miller DL, Rosekind MR. Flight crew fatigue II: short-haul fixed-wing air transport operations. *Aviat Space Environ Med*. 1998;69(9 Suppl):B8–15.
25. Deacon S, Arendt J. Adapting to phase shifts, II. Effects of melatonin and conflicting light treatment. *Physiol Behav*. 1996;59(4–5):675–682.
26. Khalsa SB, Jewett ME, Cajochen C, Czeisler CA. A phase response curve to single bright light pulses in human subjects. *J Physiol*. 2003;549(Pt 3):945–952.
27. St Hilaire MA, Gooley JJ, Khalsa SB, Kronauer RE, Czeisler CA, Lockley SW. Human phase response curve to a 1 h pulse of bright white light. *J Physiol*. 2012;590(Pt 13):3035–3045.
28. Dijk DJ, Lockley SW. Integration of human sleep-wake regulation and circadian rhythmicity. *J Appl Physiol*. 2002;92(2):852–862.
29. Thorne H, Hampton S, Morgan L, Skene DJ, Arendt J. Differences in sleep, light, and circadian phase in offshore 18:00–06:00 h and 19:00–07:00 h shift workers. *Chronobiol Int*. 2008;25(2):225–235.
30. Reinberg A, Andlauer P, De Prins J, Malbecq W, Vieux N, Bourdeleau P. Desynchronization of the oral temperature circadian rhythm and intolerance to shift work. *Nature*. 1984;308(5956):272–274.
31. Quera-Salva MA, Guilleminault C, Claustrat B, Defrance R, Gajdos P, McCann CC, et al. Rapid shift in peak melatonin secretion associated with improved performance in short shift work schedule. *Sleep*. 1997;20(12):1145–1150.
32. Weibel L, Spiegel K, Gronfier C, Follenius M, Brandenberger G. Twenty-four-hour melatonin and core body temperature rhythms: their adaptation in night workers. *Am J Physiol*. 1997;272(3 Pt 2):R948–R954.
33. Smith MR, Eastman CI. Shift work: health, performance and safety problems, traditional countermeasures, and innovative management strategies to reduce circadian misalignment. *Nat Sci Sleep*. 2012;4:111–132.
34. Flynn-Evans EE, Shekleton JA, Miller B, Epstein LJ, Kirsch D, Brogna LA, et al. Circadian Phase and Phase Angle Disorders in Primary Insomnia. *Sleep*. 2017;40(12).
35. de Mello MT, Esteves AM, Pires ML, Santos DC, Bittencourt LR, Silva RS, et al. Relationship between Brazilian airline pilot errors and time of day. *Braz J Med Biol Res*. 2008;41(12):1129–1131.
36. Golden L. Irregular Work Scheduling and Its Consequences. Economic Policy Institute; 2015 [Contract No.: Briefing Paper #394].
37. Reason J. Human error: models and management. *BMJ*. 2000;320(7237):768–770.
38. Lunn RM, Blask DE, Coogan AN, Figueiro MG, Gorman MR, Hall JE, et al. Health consequences of electric lighting practices in the modern world: A report on the National Toxicology Program's workshop on shift work at night, artificial light at night, and circadian disruption. *Sci Total Environ*. 2017;607–608:1073–1084.
39. Bei B, Seeman TE, Carroll JE, Wiley JF. Sleep and Physiological Dysregulation: A Closer Look at Sleep Intraindividual Variability. *Sleep*. 2017;40(9).