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Circadian Phase, Sleepiness, and Light Exposure Assessment in Night Workers With and Without Shift Work Disorder

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Most night workers are unable to adjust their circadian rhythms to the atypical hours of sleep and wake. Between 10% and 30% of shiftworkers report symptoms of excessive sleepiness and/or insomnia consistent with a diagnosis of shift work disorder (SWD). Difficulties in attaining appropriate shifts in circadian phase, in response to night work, may explain why some individuals develop SWD. In the present study, it was hypothesized that disturbances of sleep and wakefulness in shiftworkers are related to the degree of mismatch between their endogenous circadian rhythms and the night-work schedule of sleep during the day and wake activities at night. Five asymptomatic night workers (ANWs) (3 females; [mean ± SD] age: 39.2 ± 12.5 yrs; mean yrs on shift = 9.3) and five night workers meeting diagnostic criteria (International Classification of Sleep Disorders [ICSD]-2) for SWD (3 females; age: 35.6 ± 8.6 yrs; mean years on shift = 8.4) participated. All participants were admitted to the sleep center at 16:00 h, where they stayed in a dim light (<10 lux) private room for the study period of 25 consecutive hours. Saliva samples for melatonin assessment were collected at 30-min intervals. Circadian phase was determined from circadian rhythms of salivary melatonin onset (dim light melatonin onset, DLMO) calculated for each individual melatonin profile. Objective sleepiness was assessed using the multiple sleep latency test (MSLT; 13 trials, 2-h intervals starting at 17:00 h). A Mann-Whitney *U* test was used for evaluation of differences between groups. The DLMO in ANW group was 04:42 ± 3.25 h, whereas in the SWD group it was 20:42 ± 2.21 h ($z = 2.4$; $p < .05$). Sleep did not differ between groups, except the SWD group showed an earlier bedtime on off days from work relative to that in ANW group. The MSLT corresponding to night work time (01:00–09:00 h) was significantly shorter (3.6 ± .90 min: [M ± SEM]) in the SWD group compared with that in ANW group (6.8 ± .93 min). DLMO was significantly correlated with insomnia severity ($r = -.68$; $p < .03$), indicating that the workers with more severe insomnia symptoms had an earlier timing of DLMO. Finally, SWD subjects were exposed to more morning light (between 05:00 and 11:00 h) as than ANW ones (798 vs. 180 lux [M ± SD], respectively $z = -1.7$; $p < .05$). These data provide evidence of an internal physiological delay of the circadian pacemaker in asymptomatic night-shift workers. In contrast, individuals with SWD maintain a circadian phase position similar to day workers, leading to a mismatch/conflict between their endogenous rhythms and their sleep-wake schedule. (Author correspondence: vgumeny1@hfhs.org)

Keywords: circadian adjustment, circadian phase, Light exposure at night, Melatonin, MSLT, Night work, permanent night workers, Shiftwork, shiftwork disorder, sleep, sleepiness

INTRODUCTION

Not all night workers are able to cope with sleep-wake problems associated with a night-work schedule. The circadian rhythm is relatively slow in adjusting to night work with a rate of ~ 1 h/d (Barnes et al., 1998; Folkard et al., 1991) in naturalistic night-work settings, thereby 60–70% of night-shift workers (duty schedule 19:00–07:00 h) experience difficulties with falling asleep, staying asleep, poor quality of sleep, short sleep duration, or difficulties staying awake during working hours (Knauth et al., 1980). The rapid changes in timing of the sleep-wake cycle due to work schedule, lack of environmental time cues (light/dark) for encouraging circadian adjustment, relatively slow rate of circadian adjustment, and individual differences (chronotype, vulnerability to sleep loss, family and social activity) may result in 10–30% of shiftworkers developing shift work disorder (SWD) (Drake et al., 2004; Waage et al., 2009).

Identifying the factors that give rise to SWD in shiftworkers is important because excessive sleepiness, for example, has been implicated as a contributing factor in work-related accidents (Lombardi et al., 2010; Ohayon et al., 2010; Riedel et al., 2011) and catastrophes, including Bhopal, Three Mile Island, Chernobyl, the Rhine chemical spillage, and Exxon Valdez (Mitler et al., 1988; Williamson et al., 2011). There is also accumulating evidence that SWD

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has significant negative impact on neurocognitive function and behavior, including increased risk for accidents, medical conditions, and cognitive changes (Åkerstedt & Wright, 2009; Drake et al., 2004; Gumenyuk et al., 2010). These studies emphasize the need to better understand the underlying differences in circadian physiology of shift-workers with and without SWD.

The circadian system regulates the timing of daily variations in numerous behavioral, endocrine, and neurophysiological processes (Herichova et al., 2007; Holzberg & Albrecht, 2003; Zhang et al., 2009). The daily rhythm of melatonin secretion was shown to be a reliable marker of the circadian clock (Revell et al., 2005b), and the onset of melatonin secretion under dim light (DLMO) is used as a measure of circadian phase position (Lewy & Sack, 1989). In a study by Sack et al. (1992), the DLMO in day-active participants aged 31.6 ± 12.9 yrs (mean ± SD) occurred at 21:31 h ± 55 min; a similar time of onset of melatonin secretion (21:41 h ± 29.6 min [mean ± SEM]) was found by Roden et al. (1993) in day-working individuals 27.6 ± 1.2 yrs of age. However, night workers may have an altered timing of melatonin onset due to internal circadian adjustment to their night-work and daytime sleep/light schedule (for review see Folkard, 2008). Thus, it is hypothesized that the disturbances of sleep and wakefulness in shiftworkers are related to the degree of mismatch between their endogenous circadian rhythms and night-work schedule of sleep during the day and wake activities at night.

In simulated night-work studies, individuals who delay their internal circadian rhythms to a compromise phase position (delay by ~7 h with respect to their day-oriented circadian phase) to more appropriately match their sleep-wake schedule have improved sleep-wake function (Smith et al., 2009). In this study, the compromise circadian phase position was effectively achieved in 8 out of 9 subjects during a well-controlled laboratory protocol, i.e., light exposure was restricted during morning hours, exposure to bright light occurred during the simulated night shift, and time for sleep and brief exposure to outside light during afternoon hours were scheduled for each day through entire the study. In contrast to that experimental group, the control group had unrestricted sleep and light exposure. Four out of 10 subjects in the control group did obtain the same compromise circadian phase as was obtained by 90% of participants in the experimental group. This result suggests a natural process of adjustment of circadian rhythms in some individuals in response to night work, however, with much less efficiency compared to individuals using appropriately timed bright light and sleep.

In naturalistic night-shift work studies, shift of internal circadian phase also may occur, but findings are mixed (Boivin & James, 2002; Madokoro et al., 1997; Roden et al., 1993; Sack et al., 1992; Weibel et al., 1997). Discrepancies between studies may relate to type and duration of shifts, or other factors, e.g., light exposure, intrinsic period, etc. Also, it is very important to take into account the different approaches used to evaluate circadian phase. In some studies, authors used acrophase (peak) of the melatonin amplitude, whereas in other studies DLMO was used. Differences between these two types of methods can contribute to the mixed results found in the current literature. For example, Roden and colleagues (1993) found minimal variation (1/9) in the timing of melatonin onset in permanent night workers relative to day-working controls (22:04 h ± 27.2 min and 21:41 h ± 29.6 min, respectively). In the study by Boivin et al. (2002), night-shift-working nurses showed spontaneous delays of their circadian rhythms of melatonin (midpoint measure) by 5 h after 12 night shifts as compared to that after 10 d of vacation of a day-active schedule. In a study by Madokoro et al. (1997), where no changes in melatonin timing relative to day workers were seen, participants only worked four night shifts/mo (never consecutively), which likely prevented any shifts in the timing of the circadian pacemaker. In contrast, Sack et al. (1992) studied night workers who regularly worked two to five consecutive night shifts and found significant variability across subjects in the timing of plasma melatonin onset relative to day workers. In that study, 5/9 night workers had an afternoon melatonin onset (13:43–15:18 h), 3/9 had morning onset (10:28–12:00 h), and 1 worker had onset at 24:30 h. In another study of nurses working three consecutive night shifts, timing of melatonin secretion (evaluated by acrophase) was also variable, between 12:08 and 06:36 h, and, yet, different from day workers (Quera-Salva et al., 1996). In the night workers of that study, two groupings of peak melatonin timing were identified, with one group (n = 6) having a peak around noon (mean =12:08 h) and the other group (n = 13) having a peak in the early morning (mean = 06:36 h), whereas day-working nurses showed an acrophase of melatonin at 04:40 h ± 20 min. Finally, in the study of Weibel et al. (1997), the onset of plasma melatonin collected under <100 lux among permanent night workers varied between 21:45 and 05:05 h. In that study, 7 out of 11 subjects delayed the acrophase of melatonin with respect to the control, day-working group. Among these seven night workers, four were able to obtain a compromise circadian phase position, with onset of melatonin secretion between 02:30 and 05:00 h, which probably also favored their daytime sleep occurring between 07:00 and 15:00 h for days on the shift. Based on these studies and a review by Folkard (2008), it is possible that in natural night-work settings, some individuals are better able to adjust the timing of their endogenous circadian clock to align more closely with the night-work schedule than others. The degree of circadian mismatch may be associated with the development of sleep-wake symptoms and specifically SWD.

Because previous studies in shiftworkers did not relate the degree of phase shifting to sleep-wake symptoms and the associated diagnosis of SWD, it is important to determine if the sleep-wake disturbances experienced by shift-workers (i.e., SWD) are related to the phase of the circadian pacemaker. To our knowledge, no studies

have addressed the presence or absence of meeting SWD diagnostic criteria in relation to the timing of melatonin secretion in permanent night workers. Lack of an appropriate shift in circadian phase in response to night work may be a critical factor in the development of SWD. However, it is not known if individuals with SWD have phase differences relative to asymptomatic shiftworkers. Given the variability in circadian phase found in previous studies of shiftworkers, combined with findings from simulated shiftwork studies showing improvement of sleep-wake function related to circadian delays, we hypothesize that patients with SWD (symptomatic night workers) fail to delay their internal circadian phase to align with their sleep-wake schedule imposed by night work. The present study used 25-h dim light melatonin profiles to test for phase differences between patients diagnosed with SWD compared to asymptomatic night-shift workers (ANWs). We hypothesize that night workers with SWD will have an earlier circadian phase, i.e., minimal to no shift, compared to asymptomatic night workers. Thus, asymptomatic shiftworkers are hypothesized to have a relative delay in their circadian rhythms compared to shiftworkers with SWD.

MATERIALS AND METHODS

The study was conducted February through April 2011. Five asymptomatic night workers (ANW) (3 females; mean ± SD age: 39.2 ± 12.5 yrs; mean yrs on shift = 9.3) and five night workers meeting diagnostic criteria (International classification of sleep disorders [ICSD]-2) for SWD (3 females; mean ± SD age: 35.6 ± 8.6 yrs; mean yrs on shift = 8.4) participated. All subjects were currently working the night shift, which started between 19:00 and 22:00 h and ended between 07:00 and 08:00 h, consisting of least 3 consecutive shifts/wk and were free of neurological and psychiatric disorders (for more details, see Table 1). All participants were required to pass a health screening, including physical examination, an interview with clinical psychologist, blood and urine chemistries, illicit drug use tests, and several questionnaires: morningness-eveningness (Horne & Östberg, 1976), Epworth Sleepiness Scale (ESS; Johns, 2000), Insomnia Severity Index (ISI; Bastien et al., 2001), Berlin questionnaire to screen out sleep apnea with each participant endorsing <2 categories on the Berlin indicating low risk for obstructive sleep apnea (OSA; Netzer et al., 1999), and Profile of Mood States questionnaire (POMS; McNair, 1992). All subjects were free of medications for a minimum of 2 wks prior to study. The mean ± SD body mass index (BMI) was 24.6 ± 6.2 kg/m^2 (ANW) and 25.7 ± 6.5 kg/m^2 (SWD) (see Table 1). All subjects who were eligible for the study had to be nonsmokers, with caffeine use ≤750 mg/d.

For SWD subjects, the inclusion criteria for the study were: ESS >10, and/or insomnia as determined by the *Diagnostic and Statistical Manual for Mental Disorders Fourth Edition* (DSM-IV) criteria in addition to having an ISI ≥11. In the ANW group, subjects could not have insomnia symptoms more than once per week or an ESS outside the normal range (ESS < 10) (Table 1).

All participants were asked to maintain their habitual sleep schedule during the day of the study and have at least three consecutive work nights immediately prior to the study night. All participants were asked to record their habitual sleep habits in a sleep diary for 2 wks prior to the laboratory study. Two ANW and two SWD participants slept in the sleep center during their normal daytime sleep schedule immediately prior to the study, as their usual wake times were too close to the study start time to permit travel to the sleep center in time for their first melatonin assessment. In addition to a sleep diary, all participants were asked to wear an Actiwatch (Respironics Actiwatch-L; Philips, Guildford, Surrey, UK) on their nondominant wrist for 2 wks in order to collect rest-activity and light-exposure data. Actigraphy is a widely used method to determine whether a person is sleep/awake, and some can collect light exposure data as well (Ancoli-Israel et al., 2003). All participants were instructed to keep the sleeve from covering the light sensor of the watch. Actigraphy data corresponding to periods on night shift were extracted and calculated

TABLE 1. Means (M) and standard deviations (SD) of parameters obtained during clinical evaluation

Parameters	Asymptomatic night workers	Night workers with SWD	*p* level
Age	39 yrs 2 mo ± 12 yrs 5 mo	35 yrs 6 mo ± 8 yrs 6 mo	n.s.
Race	All Caucasian	3 Caucasian, 2 African American	
BMI	24.6 ± 6.2	25.7 ± 6.5	n.s.
ESS	5.2 ± 2.6	13.2 ± 2.9	.01
ISI	4.8 ± 2.1	11.8 ± 4.0	.01
M-E	45.5 ± 12.9	53.2 ± 8.8	n.s.
Duration (mos) on night shift	Range: 24 – 300 M ± SD: 124 ±111	Range: 12 – 144 M ± SD: 100.8 ± 52.7	n.s.
Duration of shift (h)	10.8 ± 1.09 h	11.2 ± 1.09 h	n.s.
Start/end time of shift	19:48 ± 01:46 h/07:15 ± 00:48 h	20:36 ± 01:48 h/07:06 ± 00:42 h	n.s.
Number of shifts/wk	4 ± 1	5 ± 2	n.s.
Nocturnal sleep/wk (number of nights)	3 ± 1	2 ± 2	n.s

BMI = body mass index; ESS = Epworth Sleepiness Scale; ISI = Insomnia Severity Index; M-E = Morningness-Eveningness Questionnaire; n.s. = $p > .05$; SWD = Shiftwork disorder.

separately from data corresponding to periods when subjects were off from work. Because one of the participants from ANW group misunderstood instructions regarding the actiwatch, actigraphy data for this participant were available only for days on the night shift.

All participants were admitted to the sleep center at 16:00 h, where they stayed in a dim light (<10 lux), sound-attenuated private room with personal bedroom and bathroom facilities for the study period of 25 consecutive hours. Subjects were aware of clock time. Continuous video and audio monitoring of the bedroom was conducted throughout the study. Participants were not allowed to sleep during the entire study and had stay out of bed, except for multiple sleep latency test (MSLT) (see below). Technicians monitored the subjects throughout the study and prevented subjects from falling asleep by talking to them or asking them to leisurely walk around the room's space (1 m^2) (not more than 2 min, and at least 20 min before saliva sampling for melatonin) if sleepiness persisted. For each saliva sample, all participants were asked to be seated in the comfortable chair and remain seated until the sample was checked and completed for the correct amount of saliva. When subjects were not completing MSLT nap trials, they were allowed to sit in a comfortable chair and watch movies, drink water or juice, and eat food that was provided for them (except for chocolate, tomatoes, caffeine, bananas, and mustard—which can interfere with melatonin assessment). Ten minutes prior to saliva sample collection, no food or drink was allowed, and subjects were asked to rinse their mouth using clean water. Toothpaste, mouthwash, as well as lipstick were not allowed during the study. Subjects were allowed to partake in other approved activities, such as reading or listening to music. If the subject wanted to watch a DVD movie, the light intensity of the laptop computer screen was maintained ≤10 lux (angle of gaze), and the distance from the subject's eyes and screen was always ≥40 cm. Participants were allowed to use their cell phones briefly, if needed for family reasons (30% of subjects had children of early and middle school age).

The study was approved by the Institutional Review Board (IRB) committee of the Henry Ford Health System and all procedures respected the ethical standards of the journal as outlined in Portaluppi et al. (2010). Prior to taking part in the study, all participants were informed about the general nature of the study and provided written consent. Participants were compensated for their participation.

Saliva samples were collected at 30-min intervals using a Salivette tube (SARSTEDT AG & Co., Nümbrecht, Germany) with cotton insert. Participants were instructed about the amount of saliva needed prior to the study. Each sample was weighed to ensure a minimum of 8.9 g of saliva before it was centrifuged. A total of 51 frozen salivary melatonin samples/participant were sent to Pharmasan Labs, Inc. (Osceola, WI, USA) to be radioimmunoassayed for melatonin. The sensitivity of the assay was 1 pg/mL; intra/interassay coefficient of variations were 12.1% and 13.1%, respectively.

DLMO was determined using the method reported by Lee et al. (2006). The threshold for DLMO was calculated for each individual melatonin profile. The average of the five lowest continuous points during the phase assessment, plus 15% of the average of the five highest continuous points was determined across the 51 samples. DLMO was defined as the time that the fitted curve (see Figure 1) rose above the individual's threshold, as long as it remained above for at least 1 h.

Objective sleepiness was assessed by the MSLT consisting of 13 trials scheduled at 2-h intervals starting at 17:00 h, using the standard research procedure of Carskadon et al. (1986). Prior to each MSLT, electrodes were checked and replaced if necessary. Thus, three full MSLTs were performed and compared between groups: evening (17:00–23:00 h), night (01:00–09:00 h), and daytime (11:00–17:00 h).

Statistical Analysis

Due to sample size and potential deviations from normality, a Mann-Whitney U test was performed for between-group comparisons. The relationship between DLMO, sleepiness (evaluated by ESS), and insomnia (evaluated by ISI) was tested using Spearman correlation coefficients. Data reported in Results are means ± SEM for the MSLT naps and means ± SD for all the other study variables.

RESULTS

Circadian Phase Differences Between ANWs and Night Workers With SWD

The melatonin rhythm profile and DLMO for each participant is presented in Figure 1. As hypothesized, ANWs had a delayed mean (± SD) DLMO of 04:42 ± 3.25 h, with reference to the mean DLMO of ~21:40 h for day-active individuals (Roden et al., 1993; Sack et al., 1992), whereas that of SWDs was 20:42 ± 2.21 h. The result of the Mann-Whitney U test comparing the ANW with the SWD group was statistically significant ($U = 1$; $z = 2.40$; $p < .02$).

Sleep

Tables 2 and 3 summarize the sleep diary data for days on and days off the night shift. For days on and off the night shift, the two groups showed no significant differences for wake time, latency to sleep, total sleep time, total time in bed, duration of awakening, and number of naps (Tables 2 and 3). There was significant difference between bedtimes for days off from work; individuals with SWD had an earlier bedtime than the ANW group ($U = 3.5$; $z = -1.8$; $p < .05$; Table 3). The number of nights worked in succession 2 wks prior to the study did not differ between groups.

There were no significant differences found between groups in activity-rest data recorded by actigraphy, except for the time in bed corresponding to days on the

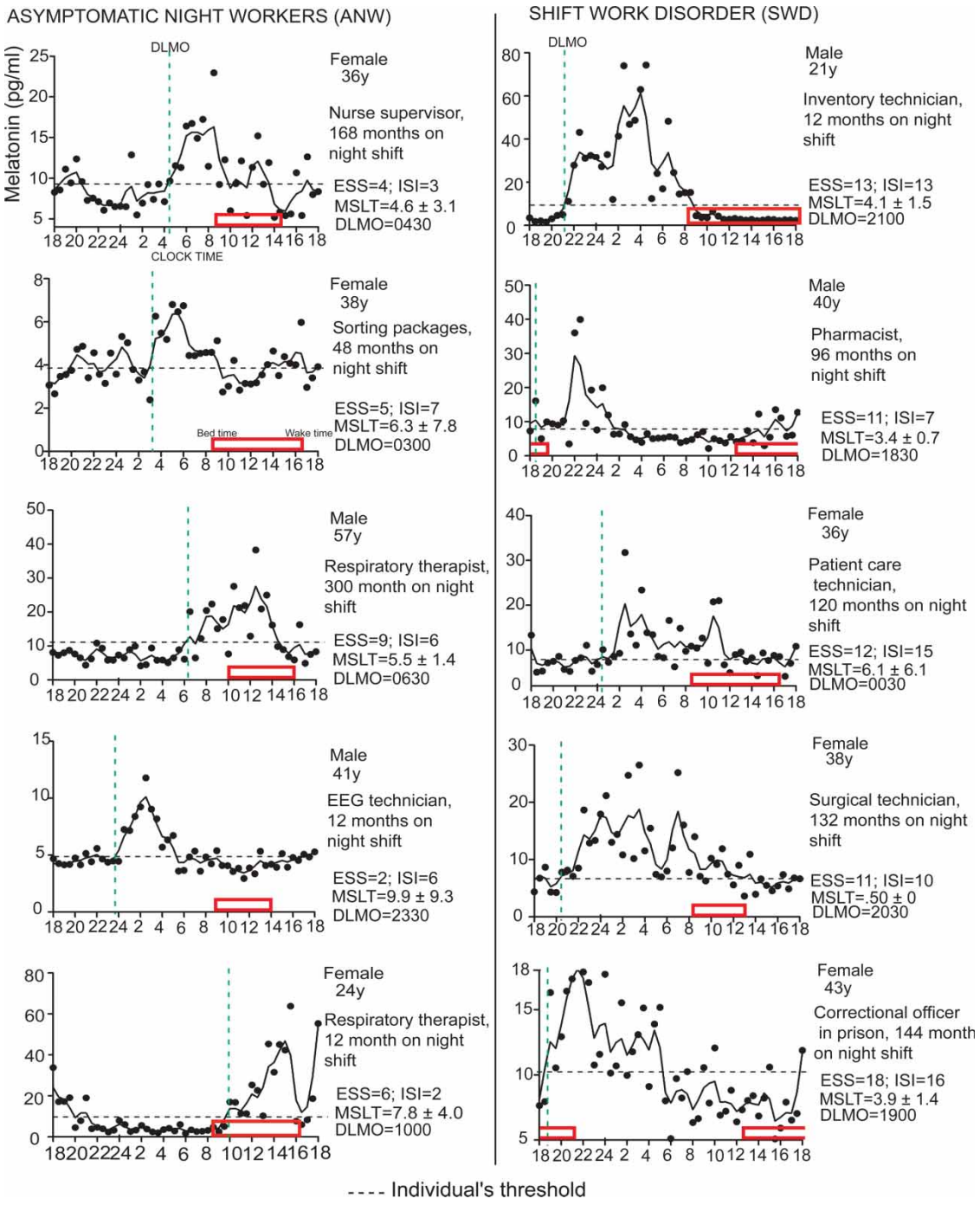

FIGURE 1. Melatonin profiles of 10 individual subjects that were determined from saliva samples collected every 30 min in dim light. Each black dot represents amount (units) of melatonin in the single saliva sample. The fitted lowess curves for each melatonin profile were generated by algorithm in GraphPad Prism software (La Jolla, CA, USA). The dashed horizontal lines of each graph represent an individual threshold calculated separately for each participant; for details see Materials and Methods. The green horizontal line represents the time of DLMO. Bed and wake times are arranged according to the mean values from sleep diary data (days on the shift) and depicted by the horizontal bar.

night shift. Individuals with SWD on average stayed in bed longer (10.2 ± 1.5 h) than ANWs (7.6 ± .6 h) across the 24-h period ($U = 1$; $z = -2.4$; $p < .01$).

MSLT

Figure 2 illustrates findings for sleep latency per group across the 24 h. The MSLT corresponding to the time of night shift (01:00–09:00 h) was significantly shorter (mean ± SEM: 3.6 ± .90 min) in the SWD than in ANW group (6.8 ± .93 min; $U = 2$; $z = 2.19$; $p < .028$). Individual sleep latency results on the MSLT corresponding to 01:00–09:00 h are presented in Figure 1. The MSLT corresponding to evening time, 17:00–23:00 h, was not significantly different (SWD: 11.2 ± 1.48 min vs. ANW: 12.23 ± 1.41 min; $U = 10$; $z = .5$; $p > .05$) between groups. There were no significant differences found between

TABLE 2. Sleep diary data (mean ± SD) for days on the night shift*

Parameter	ANW	SWD	*p* value
Bed time	08:55 h ± 43.2 min	10:12 h ± 2 h 57 min	.7
Wake time	15:45 h ± 1 h 05 min	17:10 h ± 3 h 20 min	.3
TIB	6 h 53 min ± 1 h 47 min	7 h 58 min ± 2 h 24 min	.9
TST	5 h 51 min ± 1 h 20 min	6 h 20 min ± 2 h 10 min	.9
LTS (min)	12.4 ± 14.1	11.9 ± 9.9	1
Duration (min) of awakening	6.56 ± 9.8	10.04 ± 11.5	.6
Number of naps at work	.6 ± .8	1.8 ± 2.6	.6
Number of nights worked in succession prior to study	4.2 ± 1.0	3.4 ± .8	.5

*TIB = time in bed; TST = total sleep time; LTS = latency to sleep

TABLE 3. Two-week sleep diary data (mean ± SD) for days off the night shift*

Parameter	ANW	SWD	*p* value
Bed time (individual)	1. 02:20 ± 2.3 h	1. 22:30 ±1.20 h	.05
	2. 12:15 ± 3.1 h	2. 22:50 ± 2.70 h	
	3. 01:25 ± 2.1 h	3. 23:40 ± 1.5 h	
	4. 02:00 ± 3.2 h	4. 02:00 ± 1 h	
	5. 05:00 ± 2 h	5. 23:00 ± 2.7 h	
Wake time (individual)	1. 10:10 ± 2.1 h	1. 08:10 ± 1 h	.1
	2. 07:35 ± 2.7 h	2. 06:45 ± 1.7 h	
	3. 08:55 ± 1.8 h	3. 08:40 ± 2.1 h	
	4. 11:35 ± 3 h	4. 09:00 ± 1.3 h	
	5. 13:55 ± 2.2 h	5. 10:05 ± 2.9 h	
TIB	8 h 09 min ± 39 min	8 h 55 min ± 1 h	.5
TST	7 h 40 min ± 47 min	8 h 13 min ± 1 h	.6
LTS (min)	11.5 ± 7.1	16.9 ± 11.4	.8
Duration (min) of awakening	7.58 ± 9.5	9.24 ± 9.5	.9
Number of naps at work	.6 ± .8	1.8 ± 1.5	.6

Numbers under ANW and SWD indicate subjects 1 to 5 of each group. TIB = time in bed; TST = total sleep time; LTS = latency to sleep. *p* value, Mann-Whitney *U* test.

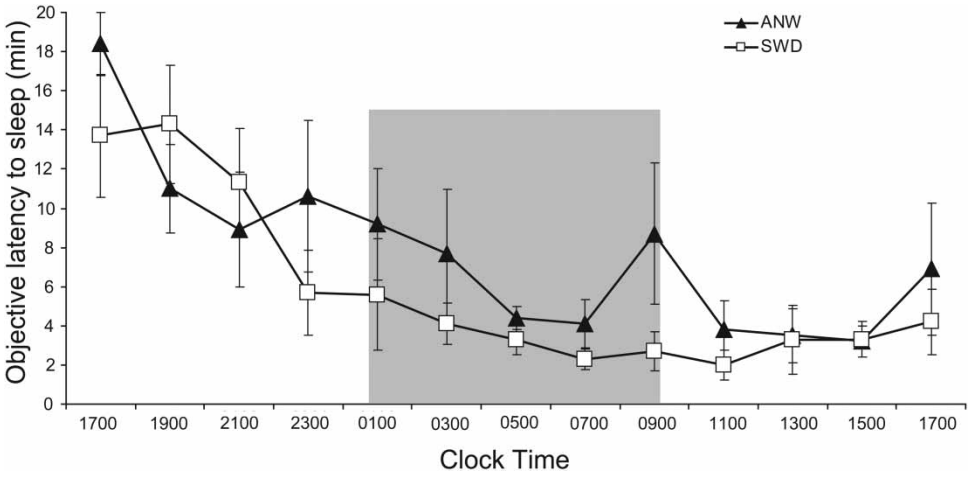

FIGURE 2. Mean sleep latency (±SEM) in minutes for each single test for each group. The means of five naps recorded between 01:00 and 09:00 h is shaded. The MSLT corresponding to these five naps was statistically different between two groups (see Results).

groups for MSLT corresponding to daytime during sleep deprivation (SWD: 3.20 ± .88 min vs. ANW: 4.35 ± 1.67 min; $U = 11.5$; z = .2; $p > .05$).

Results of Correlation analysis

Figure 3 illustrates results of the correlation analyses. The ISI obtained prior to the study during health screening was significantly correlated with the timing of the DLMO ($r = -.68$; $p < .03$), indicating that subjects with more severe insomnia symptoms had an earlier DLMO. DLMO was not significantly correlated with the ESS obtained prior to the study during health screening ($r = -.55$; $p < .09$), but there was a trend for sleepier subjects to have earlier DLMO times (Figure 3).

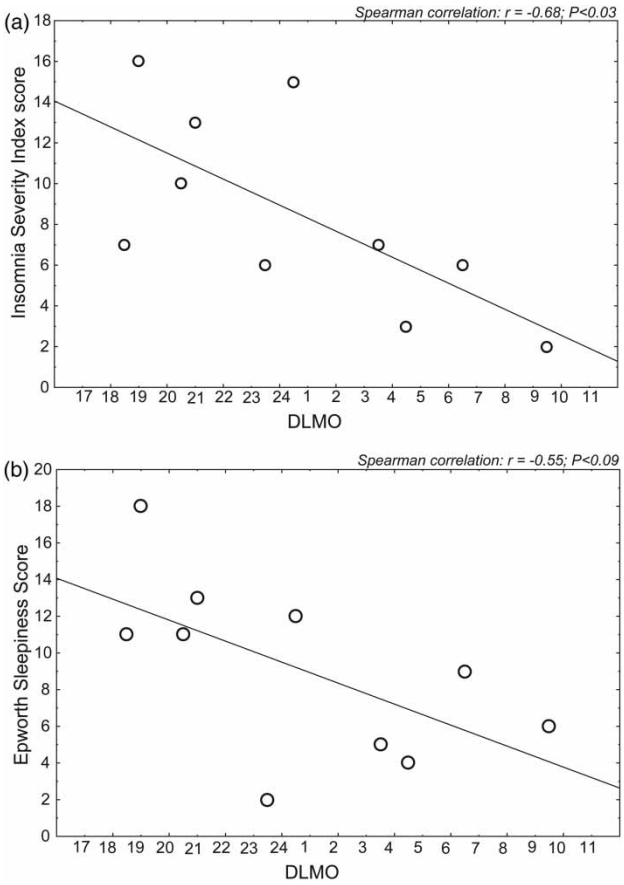

FIGURE 3. Illustration of Spearman's correlation analysis performed for (a) DLMO and insomnia severity (ISI) and (b) DLMO and excessive sleepiness (ESS) for all participants.

Light Exposure Evaluation

Light exposure was recorded by the Actiwatch-L for 2 wks prior to the laboratory study. Overall, daily light exposure across each 24-h period corresponding to a work day for the 2 wks did not significantly differ between the two groups. Previously published simulated night-shift work studies showed that if time for light exposure is inappropriate relative to the phase response curve to light, the circadian clock can be shifted in the wrong direction (Mitchell et al., 1997; Revell & Eastman, 2005a) and opposes phase delay, e.g., due to light exposure during morning hours (Eastman et al., 1994). Therefore, a secondary analysis of two time windows for light exposure (for working days) that corresponded to 23:00–04:00 h and 05:00–11:00 h was performed and results compared between groups. There was significant difference between night workers with SWD and ANWs for light exposure. Individuals in the SWD group were exposed to more light during the morning hours, i.e., 05:00–11:00 h, than the ANW group (798 ± 378 lux vs. 180 ± 120 lux, respectively; $U = 5$; $z = -1.8$; $p < .05$), whereas for light exposure in the time window corresponding to 23:00–04:00 h, there was no difference between groups (140 ± 150 lux vs. 105.3 ± 58 lux, respectively; $p > .05$).

DISCUSSION

The results of our study showed that four out of the five ANW subjects delayed their circadian rhythm of melatonin by more than 7 h relative to the group with SWD when on the night shift. The difference in DLMO between groups was 8 h (ANW: 04:42 ± 3.25 h vs. SWD: 20:42 ± 2.21 h). With the evaluation of the circadian phase from a single circadian cycle, this difference in phase between groups was robust and statistically significant. The phase of individual's melatonin rhythm of day workers has been found to be relatively stable (Dawson et al., 1992; Revell et al., 2005b) and, therefore, is a reliable circadian phase marker. However, it is not known if this is the case for night-shift-working individuals, who frequently experience irregular sleep-wake cycles and light/corresponding to periods of night work in shiftworkers, are needed to determine the stability of the phase differences observed in this study. From previous studies (Dumont et al., 2001; Sack et al., 1992; Weibel et al., 1997), it was shown that some night workers are able to delay their circadian rhythms naturalistically, whereas others are not. The mechanism of this adjustment in real-world settings is still unknown, but simulated night-shift work studies were able to demonstrate such factors as appropriately timed light and dark exposure that are the main factors contributing to phase shifts in response to night work. Our results are consistent with these studies in that attenuation of light exposure during the morning hours (05:00–11:00 h) and relatively late bedtimes on days off from work were found in the ANW group to likely contribute to the phase delays observed in this group. However, in individuals with SWD, both of these factors—more light exposure in the morning and earlier bedtimes when off from work—may have limited any potential circadian phase delays.

In our previously published study (Gumenyuk et al., 2010), we demonstrated a deficit in a neurophysiological index of sensory memory as well as attention-dependent brain activity in patients with SWD compared to asymptomatic night workers. In the present study, we found that clinical symptoms of SWD are associated with a failure to shift melatonin secretion in response to night work. These results further validate SWD as a circadian disorder (Sack et al., 2007), with impact on memory- and attention-dependent neuronal activities.

The present study emphasizes the need for increased attention to the problem of shiftworkers with symptoms of excessive sleepiness and/or insomnia as signs of their inability to cope with night-work requirements that can ultimately lead to unsafe work- and after-work-hour situations. Among shiftworkers, there is a particular subset of night workers, those who meet diagnostic criteria for SWD, who may benefit from focused circadian interventions aimed at inducing circadian phase delays. For example, a recent laboratory study showed that bright light during the early part of a simulated night

shift, wearing dark sunglasses when outside, sleeping in a dark bedroom at scheduled times, and a "light brake" in the afternoon were able to maintain stable circadian phase (Smith et al., 2009). Similar positive results of circadian interventions have also been reported in shift-workers in uncontrolled work environments (Czeisler et al., 1982). Moreover, applying appropriate diagnostic principles to identify individuals with SWD will facilitate detection of those night-shift workers who will need and who will most benefit from recommended circadian interventions for sleep-wake disturbances.

In contrast to the shift-work-disordered persons, asymptomatic shiftworkers are unlikely to benefit from intervention in circadian adjustment because they naturalistically obtain an appropriate compromise phase position in response to night work. Our results suggest that low light exposure during the morning hours and later bedtimes on days off from work provide potential explanation for the asymptomatic sleep-wake profile of the ANW group. In SWDs, morning light occurs after the estimated time of minimum core body temperature (DLMO + 7 h), whereas in ANWs the morning light occurs before their minimum core body temperature. That difference in light exposure may result in opposite phase responses in these two groups, with SWD subjects having phase advances and ANWs having phase delays. Another factor that may contribute to oppose the phase delay in individuals with SWD is their earlier bedtime as compare to asymptomatic workers for days when they are off from work. In addition, other factors, e.g., vulnerability to sleeping at an adverse circadian phase and intrinsic period (τ), may play a role in changes of circadian rhythms in response to night-work schedules and should be the focus of further investigations.

Finally, sleepiness assessed by MSLT in the current study showed a range of individual sleep latencies between 5 and 10 min in ANWs vs. .50 and 6 min in SWD patients between 01:00 and 09:00 h—a time span corresponding to their night shift. It is likely that circadian misalignment contributes to the higher sleep tendency in individuals with SWD during night work. In day-active individuals, the nocturnal sleep latency range is between 3 and 7 min (Buysse et al., 2005; Richardson et al., 1982). Lack of significant differences in total sleep time between groups in our study is further support that the short nocturnal sleep latency in individuals with SWD is likely due to circadian misalignment.

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