

and a shorter interval between DLMO and waketime ( $p < 0.05$ ). However, the decay rate was similar between chronotypes and was not associated with sleep schedule parameters. No difference appeared between chronotypes with extreme phases and no significant correlation was found between individual estimates of SWA decay and sleep schedule.

**Conclusion:** These results support the assumption that in some individuals, differences in homeostatic regulation are at the origin of morningness-eveningness preference and are directly related to the resulting differences in the phase angle between circadian phase and sleep schedule.

**Support (optional):** Canadian Institutes of Health Research

## 0142

### PSYCHO-BEHAVIORAL PREDICTORS OF CHRONIC JET-LAG IN LONG-HAUL AIR CREW

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**Introduction:** Although long-haul air crew report significant chronic jet-lag, a discordance between their levels of objective and subjective jet-lag exists. The extent to which psychological and behavioral variables mediate this discordance is of importance in the diagnosis and treatment of circadian rhythm disorders. Additionally, a major confounding factor is the self-selected nature of this type of sample by which predispositional factors may influence occupational choice. The aim of the present study was to examine the role of psychological and behavioral factors in reports and experienced jet lag.

**Methods:** In a prospective design, ten long-haul air crew completed measures of well-being, sleep (actigraphy and diary), coping, chronotype, and perceptions of jet lag, before, during and after a long-haul flight. Additionally, melatonin was assayed over the course of the study. A comparison group, matched for age, gender, and length of working week, were used to compare predispositional factors.

**Results:** Although there was a discrepancy between objective and subjective jet-lag, most psychological characteristics failed to mediate the relationship. However, a relationship between coping style and perceptions of jet-lag was observed as was increased fatigue related to decreased well-being ( $r = -0.68$ ,  $p < 0.05$ ) and extent of time change to sleep-onset latency ( $r = -0.86$ ,  $p < 0.05$ ). There were no differences between groups on well-being ( $t(18) = 0.78$ , n.s.), chronotype ( $t(18) = 0.43$ , n.s.) or coping style. However, differences between the groups were observed on sleep-onset latency ( $U = 8.5$ ,  $Z = 3.36$ ,  $p < 0.005$ ) on "nights off" from work.

**Conclusion:** The findings demonstrate that whereas predispositional and psychological factors are not involved in choosing a career as long-haul air crew, they are related to the experience of jet-lag. The results are discussed in relation to the psycho-social aspects of frequent long-haul travel and in psychological characteristics in occupational choice amongst air crew.

**Support (optional):** None

## 0143

### WHY DO SOME PEOPLE SECRETE MORE MELATONIN THAN OTHERS?

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**Introduction:** Melatonin is secreted from the pineal gland at night. Low levels of melatonin are associated with greater risk for cancer and cancer growth. Thus, we looked for factors that influence melatonin levels.

**Methods:** Melatonin secretion (area under the curve, AUC) was

estimated from baseline melatonin profiles derived from saliva samples collected half-hourly for 20 hours in dim light ( $< 10$  lux) from 85 males and 86 females. Subjects were young (18-45y) nonsmokers with no medical, psychiatric or sleep disorders, and were medication free (except hormonal birth control,  $n = 15$ ). Prior to saliva collection subjects abstained from alcohol for at least 24 hours, and avoided NSAIDs and were on fixed sleep schedules for at least 3 days.

**Results:** Peak melatonin levels ranged from 2.4 to 83.6 pg/ml. AUC ranged from 88 to 2126 pg/ml/h. Females tended to secrete more melatonin ( $p = 0.06$ ), because hormonal birth control increased melatonin ( $p = 0.024$ ). Drinking 10 or more alcoholic drinks per week was associated with secreting less melatonin ( $p = 0.02$ ). Full-time workers secreted less melatonin ( $p = 0.03$ ) than students, part-time workers and those unemployed. Definite morning types secreted less melatonin than other morningness-eveningness types ( $p = 0.047$ ). There was a trend for people who wore eyeglasses and/or contact lenses to secrete more melatonin ( $p = 0.06$ ,  $p = 0.07$ ) than people without corrective vision. There were no significant associations between melatonin secretion and race, education, Epworth, PSQI, MMPI-2 scores, and the presence of bed partner and/or housemate.

**Conclusion:** Several factors may influence melatonin levels. Potential mechanisms include that full-time workers and definite morning types may receive light that suppresses their melatonin, and that this photoperiodic history is reflected in their subsequent dim light melatonin profiles. UV filters in corrective vision may reduce exposure to short wavelength light which can suppress melatonin. The causes of the large variation in melatonin levels remain unknown and are probably genetic.

**Support (optional):** RO1 NR007677, RO1 OH003954, RO1 NS35695, RO1 NS23421

## 0144

### SCHEDULED BRIGHT LIGHT AND DARKNESS TO ACHIEVE A COMPROMISE PHASE POSITION FOR PERMANENT NIGHT SHIFT WORK

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**Introduction:** This is the second in a series of studies designed to achieve and maintain a compromise phase position for permanent night shiftwork, in which the sleepest time of the circadian cycle is delayed out of the night work period and into the first half of daytime sleep, improving night shift alertness and subsequent daytime sleep, but not precluding late nighttime sleep on days off.

**Methods:** All subjects underwent 3 consecutive night shifts (23:00-7:00) followed by two days off. An experimental group ( $n = 9$ ) received five 15-minute light pulses ( $\sim 3,200$  lux,  $\sim 1,100 \mu W$ ) beginning at 23:45, interspersed by 45 minutes of room light. They wore sunglasses ( $\sim 15\%$  transmission) when outside. Sleep in darkened bedrooms was from 8:30-15:30 after the first two night shifts, 8:30-13:30 after the third night shift, and 3:00-12:00 on days off. Subjects went outside for  $\geq 15$  minutes after awakening to receive a "light brake" to keep them from delaying past the compromise phase position, a delay of  $\sim 6$  h. A control group ( $n = 12$ ) remained in room light during night shifts, wore sunglasses ( $\sim 37\%$  transmission), and had unrestricted sleep and outside light exposure. The dim light melatonin profile was collected before and after night shifts and days off to measure the phase shift.

**Results:** Phase delays of the melatonin onset for the experimental group were larger than for the control group ( $4.2 \pm 0.8$  vs  $0.9 \pm 1.2$  h,  $p < .001$ ).

**Conclusion:** Our previous study showed a delay of  $\sim 3$  h after two night shifts with bright light. This study found a similar delay of  $\sim 4$  h after

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three night shifts and two days off. While the compromise position has not yet been reached, a relatively delayed circadian phase was maintained after two days off. More night shifts will be required to achieve the compromise phase position.

**Support (optional):** R01 OH003954 to C.I.E.

### 0145

#### ENTRAINMENT OF *HPER2* EXPRESSION IN PERIPHERAL BLOOD MONONUCLEAR CELLS FOLLOWING SIMULATED NIGHT SHIFT WORK.

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**Introduction:** Judicious light and darkness exposure throughout the day can promote the appropriate alignment of the endogenous hormonal rhythms to night shift work. However, the synchronization of human peripheral circadian oscillators to shifted sleep-wake schedules is currently unknown. We evaluated *HPER2* expression in peripheral blood mononuclear cells (PBMCs) with respect to the simultaneous resetting of the plasma cortisol rhythm throughout simulated night shift work.

**Methods:** Five healthy candidates (4 male, 1 female in follicular phase) aged (mean  $\pm$  SD) 24.9  $\pm$  4.8 years maintained stable sleep and meal schedules before the study start. Upon admission to the laboratory, sleep/wake schedules were delayed by 10 hours to simulate nighttime "work". The light intervention included exposure to full-spectrum white light of (mean  $\pm$  SEM) 6,036  $\pm$  326 lux during 8-hour night shifts and dim light exposure after each night shift with the use of sunglasses (5% visual light transmission). *HPER2* expression in PBMCs and plasma cortisol concentration were estimated from 24-hour blood sampling periods performed before and after nine simulated night shifts. The expression of *HPER2* in isolated PBMCs was determined relative to *HCDK4* via real-time PCR.

**Results:** Following nine simulated night shifts, the cortisol rhythm was delayed by 10.2 hours and the fitted maximum of cortisol expression occurred (mean  $\pm$  SEM) 3.5  $\pm$  0.7 hours after awakening. Dual-harmonic regression analyses revealed that all participants demonstrated significant circadian rhythmicity in *HPER2* expression. Peak *HPER2* expression occurred 0.6  $\pm$  0.7 hours after awakening and was in a conventional temporal relationship with the sleep/wake cycle, even though it was shifted.

**Conclusion:** This is the first demonstration of the entrainment of peripheral circadian oscillators in PBMCs to an atypical sleep-wake schedule. In light of recent evidence implicating peripheral oscillators and tissue function, this line of investigation may have important implications for understanding the medical disorders affecting night shift workers.

**Support (optional):** *Fonds de Recherche en Santé du Québec*, Canadian Institutes of Health Research.

### 0146

#### EXTENDED DURATION WORK SHIFTS AND PREVENTABLE ADVERSE EVENTS: A RISK TO PATIENTS AND PHYSICIANS

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**Introduction:** We recently reported that interns working extended duration shifts have an increased risk of motor vehicle crashes, needle

stick injuries, and medical errors. We assessed the impact of working extended duration shifts on patient safety (preventable adverse events) and the well-being of the interns themselves.

**Methods:** 2,737 physicians in their first post-graduate year participated in a nationwide web-based survey, completing 17,003 monthly reports. A regression analysis was performed to determine the relationship between the number of extended duration work shifts ( $\geq 24$  hours), reported medical errors and a self-reported measure of stress. Case crossover within-subject analysis was used to assess the association between the number of extended duration shifts worked per month and the reporting of preventable adverse events. In addition, we compared self reported stress in months with and without reported preventable adverse events.

**Results:** The reporting of medical errors and the number of extended duration shifts worked in a month were both significant predictors of stress ( $p < 0.001$ ). Compared to months in which no extended-duration shifts were worked, interns working five or more extended duration shifts had seven times greater odds (OR=7.0; 95%CI: 4.3-11) of reporting at least one fatigue-related significant medical error that resulted in an adverse patient event and reported 300 percent (OR=4.1; 95%CI: 1.4-12) more fatigue-related preventable adverse events resulting in the death of the patient. Moreover, interns who reported a medical error that resulted in an adverse patient outcome were more than 3 times as likely to report high stress (6 or 7; 7-point Likert scale) in that month (OR=3.43, 95%CI: 3.31-3.56).

**Conclusion:** These results suggest that extended duration shifts negatively impact patient safety and the well-being of medical interns. They have important public policy implications for post-graduate medical education and suggest the need for counseling or other care for interns who make medical errors.

**Support (optional):** This study was supported by grants from the National Institute for Occupational Safety and Health within the U.S. Centers for Disease Control (R01 OH07567) and by the Agency for Healthcare Research and Quality (R01 HS12032).

### 0147

#### INDIVIDUAL DIFFERENCES IN ALERTNESS AND PERFORMANCE AT NIGHT IN PATIENTS WITH SHIFT-WORK SLEEP DISORDER

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**Introduction:** Decrements in alertness and performance associated with sleep loss vary considerably among individuals and are reasonably stable within individuals. We examined interindividual variability in sleepiness and performance during the night shift in patients with shift-work sleep disorder (SWSD).

**Methods:** SWSD patients randomized to 8 weeks of placebo treatment in a study investigating the effectiveness of a drug treatment for SWSD were evaluated. MSLT, Karolinska Sleepiness Scale (KSS; range=0 to 9), and 20-minute Psychomotor Vigilance Tests (PVT) were administered during two laboratory night shifts, one at week 4 and one at week 8. The laboratory night shifts directly followed the last night of each subject's usual 3- to 5-night work week.

**Results:** Eighty-three Ss completed both laboratory nights (27 females, 56 males, mean age 39.7, range 20-62). Mean values (and range) for the week-4 and week-8 night shifts were 2.3 (0 – 11.6) and 2.4(0 – 13.2)

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