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Circadian Rhythm Disruption: A Chronic Occupational Hazard Among Flight Attendants?

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America is a nation of tired workers. In 1990, the direct U.S. costs of sleep disorders and deprivation were estimated at $15.9 billion, and the indirect costs which result in stress-related, reduced workplace productivity were estimated at $150 billion. Air travel during normal sleep hours and multiple time zone changes are an integral part of the workplace for many of the 198,000 air crewmembers employed in the United States, including about 113,700 flight attendants. Flight attendant sleep cycle/circadian rhythm disruption issues may in some ways be similar to those of shift workers, but a flight attendant's work schedule often lacks the regularity which assists a shift worker's circadian resynchronization; also, a flight attendant's work often involves rapid movement through multiple time zones, and the resultant disruption of zeitgeibers (external time cues) is different than for shift workers. Because circadian disruption may affect the hormonal balance requisite to reproductive health, it is being assessed among flight attendants in reproductive health studies which The National Institute for Occupational Safety and Health (NIOSH) is currently conducting. Our objectives were to determine whether female flight attendants are more likely than teachers (comparison group) to experience circadian disruption, as measured by melatonin production and sleep displacement, and to identify metrics of disruption for future studies of reproductive health.

Each day for one menstrual cycle, 45 flight attendants and 26 teachers kept a daily diary, collected and measured their overnight urine, and wore an activity monitor to assess sleep displacement. Relations between melatonin production, sleep parameters, and flight attendant/teacher status were analyzed with linear and multiple logistic regression. Relations between sleep displacement, melatonin, and flight history-derived variables (including time zones crossed) were examined with exploratory factor analyses.

Flight attendants experienced increased circadian disruption as measured by a higher adjusted melatonin rate variance than teachers (2.8 x 105 vs. 1.0 x 105 (ng/h)2 , respectively; p=0.04) and the likelihood of being in the highest quartile of melatonin variance (Odds Ratio = 2.3; 95% Confidence Interval: 0.6 - 9.1). Although flight attendants slept longer than teachers, models for two indices of sleep displacement indicated that flight attendants incurred significant impairment of sleep compared to teachers. In factor analysis, time zones crossed was related to both melatonin desynchronization and sleep displacement.

Flight attendants experienced increased circadian disruption, as measured by more variable melatonin rates and increased sleep displacement, than a minimally-flying comparison group. For epidemiologic studies of flight crew in which melatonin measurement is infeasible, time zones crossed is a useful indicator of both sleep displacement and melatonin desynchronization.

Rest requirements for flight attendants may address issues such as alertness, but misalignment of the sleep-wake cycle and circadian rhythms may be a chronic occupational condition which may not be readjusted fully by rest after each duty period. Although worker alertness is a key safety issue in many industries, sleep and circadian rhythm research need to be expanded to determine chronic health effects of sleep impairment and, for air crew, circadian disruption.

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Abstract for the NIOSH NORA Symposium, Washington , DC, June 23 – 24, 2003
text: 492 words (500 allowed)

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Flight attendants experienced increased circadian disruption, as measured by more variable melatonin rates and increased sleep displacement, than a minimally-flying comparison group. For epidemiologic studies of flight crew in which melatonin measurement is infeasible, time zones crossed is a useful indicator of both sleep displacement and melatonin desynchronization.

Rest requirements for flight attendants may address issues such as alertness, but misalignment of the sleep-wake cycle and circadian rhythms may be a chronic occupational condition which may not be readjusted fully by rest after each duty period. Although worker alertness is a key safety issue in many industries, sleep and circadian rhythm research need to be expanded to determine chronic health effects of sleep impairment and, for air crew, circadian disruption.

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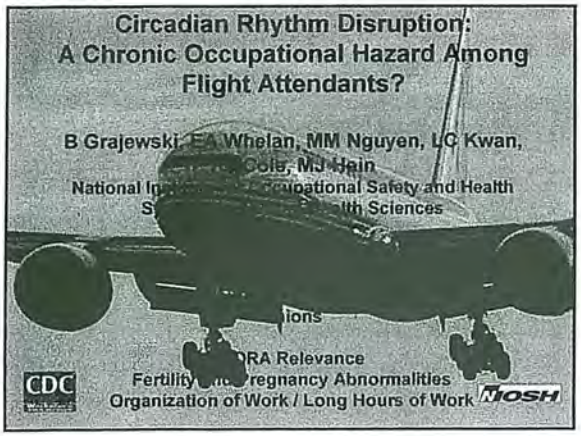
National In[illegible]ccupational Safety and Health
S[illegible]lth Sciences



[illegible]ions

[illegible]RA Relevance
Fertility [illegible] Pregnancy Abnormalities
Organization of Work / Long Hours of Work

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Background

- Flight attendants may experience increased risk of:
  - Miscarriage
  - Menstrual disorders
  - Other adverse reproductive outcomes
- Is work as a female flight attendant associated with adverse reproductive effects?

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Air Cabin Exposures

- Primary: Cosmic Radiation
  Circadian Rhythm Disruption
- Secondary: Tobacco smoke
  Ergonomic exposures
  Stress

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Assessing Circadian Rhythm Disruption

- Travel through multiple time zones:
  - ✈External desynchronization
  - ✈Internal desynchronization
  - ✈Physiologic/behavioral disturbances including sleep-wake disturbance
- Monitor sleep
- Monitor a circadian marker
- Identify useful metrics for larger studies

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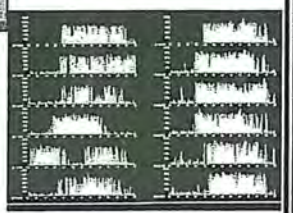
Monitor sleep



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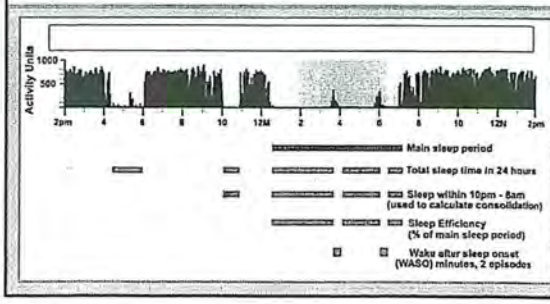
Sleep measurements:

One day's activity recorded by actigraph



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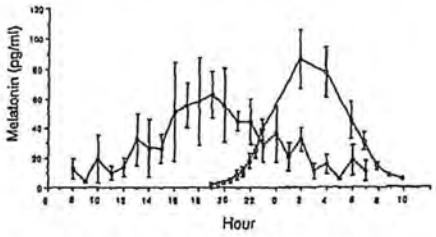
Monitor a circadian marker



Sack et al., Sleep 15(5), 1992

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Measures of Melatonin

- Overnight melatonin production rate
- Within-woman variance of overnight rate
- % Low Melatonin days (within-woman)

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Work (Flight) History Records

- Time zones crossed
  - Cumulative
  - Average / flight
- Time spent flying during normal sleep hours (10 PM – 8 AM)
  - Cumulative
  - Average / flight

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Objectives

- Determine if flight attendants are at higher risk of circadian disruption (CD) compared to teachers, as measured by melatonin production and sleep displacement
- Identify the best CD metrics for studies where biomonitoring is infeasible from
  - Melatonin
  - Sleep / activity
  - Work (flight) histories

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Methods

- 45 flight attendants, 26 teachers
- Collected and measured overnight urine for one menstrual cycle
- Daily diary
- Activity monitor
- 6-sulfatoxymelatonin measured by RIA
- Individual flight history records
- Covariates: demographics, BMI, stress, medications, exercise, cotinine, lifestyle

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Methods--analysis

- Linear and multiple logistic regression
  - Adjusted means, odds of high or low quartile
- Linear mixed-effects models for daily melatonin and sleep variables
- Exploratory principal components/factor analysis
  - Simplify 16 measures of sleep, activity, melatonin, and flight history

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Results
Actigraph Performance
Measured as Number of Actigraphs Worn

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Results
Actigraph compliance and data quality

- **94% median compliance days (range 0-100%)**
- **93% median analyzable data (range 0-96%)**

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Results
Melatonin Variance

Variance (24-hr profile)	Crude mean	Adj mean	Crude OR	Adj OR
[illegible]	[illegible]	2.8 (1.8 – 4.6)	[illegible]	2.3 (0.6 – 9.1)
T	[illegible]	1.0 (0.6 – 1.9)	1.0	1.0

Mixed Model	Within-Woman Variance	Between-Woman Variance
FA	4.3 (4.0 – 4.6)	2.7 (1.4 – 4.1)
T	2.5 (2.4 – 2.9)	5.0 (2.0 – 8.1)

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Results: Sleep Variables

Poor (lowest quartile) sleep efficiency	Crude OR	Adjusted OR
FA	1.0 (0.6 – 1.8)	1.7 (1.0 – 2.9)
T	1.0	1.0
Poor (lowest quartile) sleep consolidation	**Crude OR**	**Adjusted OR**
FA	2.5 (1.5 – 4.3)	3.0 (1.0 – 8.8)
T	1.0	1.0

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Results
Variables for PCA/Factor Analysis

- Melatonin (N=5)
- Sleep displacement and activity (N=7)
- Variables derived from flight histories (N=4)

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3 Factors Describe Circadian Disruption

1. **Sleep, Work, Time Zones (53% variance)**
   - Sleep and activity variables indicating erratic shifts of sleep and work
   - Average/cumulative time zones crossed
2. **Melatonin, Time Zones (14% variance)**
   - Melatonin rate mean and variance
   - Average/cumulative time zones crossed
3. **Melatonin and Sleep Efficiency (9.1% variance)**

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Conclusions: Circadian Disruption

- Flight attendants experience increased circadian rhythm disruption, as measured by more variable melatonin rates.
- Flight attendants incur significant impairment of sleep compared to teachers for two indices of sleep displacement.
- For studies without biomonitoring, time zones crossed is a useful indicator of both sleep displacement and melatonin desynchronization.

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" ...the 1990 direct cost of sleep disorders and deprivation may be as much as 15.9 billion dollars." (National Commission on Sleep Disorders Research)

indirect and related costs from sleep disorders/deprivation resulting in stress-related, reduced workplace productivity: $150 billion

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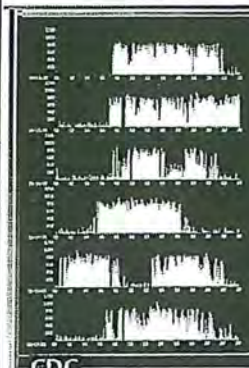

How can the workplace of 198,000 air crew (113,700 flight attendants) be improved?

Look at chronic health effects of circadian disruption

Revisit rest requirements

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Why Teachers as a Comparison Group?

- Many other groups considered
- Minimal air travel
- Few reproductive hazards
- Union membership and systematic records
- Demographic comparability

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2 Extra slides used only if discussed

Results
Sleep Variables

Total sleep time in main sleep period (hours)	Crude mean	Adj mean
FA	7.3 (7.1 – 7.6)	6.6 (6.4 – 7.2)
T	6.7 (6.4 – 6.9)	6.8 (6.5 – 6.9)

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Sleep Disturbance Among Female Flight Attendants and Teachers in a Reproductive Biomonitoring Study

B. Grajewski[1], E.A. Whelan[1], M.M. Nguyen[1], L.C. Kwan[1], and R. J. Cole[2]
[1]National Institute for Occupational Safety and Health, Cincinnati, OH 45226;
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The following pages are print images of the components of this poster, enlarged for readability of content. For presentation and integration into the poster format, please refer to the poster image. 5/30/2000

Presented at SER 2000

Abstract

Many of the 82,000 US flight attendants (FAs) may experience circadian rhythm disruption due to travel through multiple time zones. This study investigated whether FAs are at higher risk for sleep disturbance compared to teachers, as measured by questionnaire and wrist activity monitors (actigraphs). Sleep/wake cycles of 45 female FAs and 26 teachers participating in a reproductive biomonitoring feasibility study were studied. For one menstrual cycle, participants wore an actigraph, from which sleep times were estimated with a validated sleep-scoring algorithm, and kept a daily diary. Sleep parameters included total sleep minutes in the main sleep period, total sleep minutes in 24 hours, wake minutes in the main sleep period, sleep efficiency (proportion of time spent sleeping in the main sleep period), and sleep consolidation (proportion of time spent sleeping from 10 PM to 8 AM home time). Both actigraph and diary data suggest that FAs sleep longer than teachers. However, two actigraph indices of sleep disturbance indicated that FAs incurred significant impairment of sleep compared to teachers. FAs were more likely to have poor sleep efficiency (adjusted OR=1.7, CI 1.0 - 2.9) and to have poor sleep consolidation (adjusted OR=3.0, CI 1.1 -8.6). In this study, actigraphy was a feasible field method for characterization of sleep disturbance in a mobile workforce. Our observations indicate that FAs experience increased sleep disturbance, which may be an indicator of circadian rhythm disruption.

Background

- The air cabin environment is the workplace of over 97,000 flight attendants and a total of over 172,000 flight crew members.
- The scientific literature suggests that female flight attendants experience an increased risk of adverse reproductive outcomes and cancer, although the etiology of these effects remains unknown.
- Workplace exposures that may contribute to adverse health effects for flight crew include alterations of circadian rhythms and sleep quality from traveling across multiple time zones and irregular work schedules.
- NIOSH examined measures of sleep disruption within a 1995 study of 71 flight attendants and teachers (comparison group) to determine if reproductive biomonitoring studies of this highly mobile workforce were feasible.
- Public Health Impact:
  - " ...the 1990 direct cost of sleep disorders and deprivation may be as much as 15.9 billion dollars." (National Commission on Sleep Disorders Research)
  - Indirect and related costs resulting in stress-related, reduced workplace productivity: $150 billion

Study Questions

In this feasibility study, does the sleep of flight attendants differ from that of teachers (comparison group)?

- Can sleep be characterized adequately in this mobile workforce?
- How do diary and actigraphy data compare in characterizing sleep?

Methods

Participants were recruited from company and union rosters of female flight attendants and teachers aged 18-45 based in Seattle and Miami.

Participants collected daily urine and saliva samples for one menstrual cycle, and provided daily diary data for three months. Diary information on daily sleep quality was also recorded.

Sleep and wakefulness were estimated during biomonitoring with the Mini Motionlogger Actigraph System (Ambulatory Monitoring, Inc. (AMI), Ardsley, New York).

Sleep and wake information were scored according to the EEG-validated algorithm of Cole et al. (1992).

Methods--picture and caption

Actigraph and study instructions. Each study participant was asked to wear the actigraph, approximately the size of a man's wristwatch, for 24 hours/day during the biomonitoring period, removing it only for bathing or swimming.

The battery-operated, calibrated actigraph was designed to record arm motion data at 3-minute intervals. Participants were instructed to push an event marker button to electronically mark events such as wakeup time.

Analysis

Variables describing sleep (see table below) were examined descriptively; a subset of these was examined in repeated measures multivariable analyses (SAS 6.12 Proc Mixed/Proc Genmod).

Where appropriate, time data were normalized with circular transformation.

Covariate data were obtained from the baseline questionnaire, the daily diary, and cotinine biomonitoring.

Diary and actigraph data were compared. One of the measures found in both, Total Sleep Time in the Main Sleep Period, could be compared in a regression setting.

Covariate Data

Demographic data from baseline questionnaire: age, BMI, race, Hispanic origin, education, income. Age and BMI were considered potential effect modifiers.

Lifestyle data: presence of a child ≤ 4 years old at home, sharing of household duties, presence of a hostile living environment, management support, conflict between job and life goals, use of hormones, drive for thinness, body image, decision latitude (Karasek 1985), job strain (Landsbergis 1994), stress events during the study period/six months prior.

Daily diary data: sleep medications, alcohol and caffeine consumption, smoke exposure (none/passive/active), minutes of exercise outside work, number of times lifting loads ≥ 15#, job stress index, chance to relax during the week, attempt to diet during the week.

Smoking status was confirmed by daily urinary cotinine concentrations.

Methods--Sleep variables

TSTMSP	Total sleep time in the main sleep period	X	X		
WASO minutes	Minutes awake after sleep onset	X	X	X	
WASO episodes	Times awake after sleep onset	X			
TST24	Total sleep time in 24 hours		X	X	
Sleep efficiency	Proportion of sleep time inside main sleep period		X		X
Sleep consolidation	Proportion of sleep time within 10 PM – 8 AM		X		X
Latency	Time to fall asleep after "lights out"	X			
Deep sleep	"How deeply did you sleep?" 1=very lightly, 5=very deeply	X			
Sleep quality	"What was your sleep quality?" 1=very poor, 5=very good	X			
Mood	Mood on awakening; 1=very tense, 5=very calm	X			
Feelings at wakeup	1=tired and drowsy, 5=awake and alert	X			

Results

93.3% of flight attendants and 96.2% of teachers entering the study completed the biomonitoring cycle. Data collection was not diminished by work-related travel.

For many participants, the most difficult study requirement was to wear the actigraph continuously throughout the biomonitoring cycle. Also, actigraphs failed up to four times per participant, and did not record properly for 16% of all monitoring days. Despite these problems,

- Participants wore the actigraph 94% of the time (median)
- The median % analyzable data was 94% for teachers, 90% for flight attendants.

Self-reported diary TSTMSPs were an average of 39 minutes longer than actigraph TSTs, although midpoints of the main sleep period did not differ.

Self-reported WASO was an average of 63 minutes shorter than actigraph values.

Results--

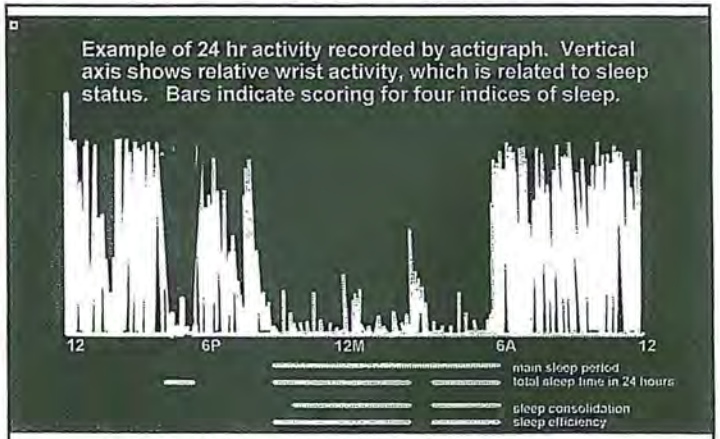
Characteristics of Flight Attendants and Teachers

Characteristic	Flight attendants (N = 45)	Teachers (N = 26)
Age (years; mean ± SD)	36.0 ± 4.7	37.4 ± 5.9
Nonwhite (%)	9.1	34.6
Hispanic origin (%)	8.9	8.0
Education: college degree or more (%)	33.3	92.3
Income: <$45,000 (%)	62.2	50.0
Body mass index (kg/m²; mean ± SD)	21.0 ± 1.6	28.8 ± 7.9
Current cigarette use, self-report (%)[1]	11.1	7.7
Daily cotinine levels: median >100 ng/mL (%)[2]	13.3	12.0
Passive smoke at work or home (%)	91.1	84.6
Caffeine (mg/day; mean ± SD)	260.9 ± 198.1	132.3 ± 105.6
Alcohol (drinks/week; N, percent)[3]		
<1	7, 16%	15, 58%
1 - 3	25, 56	8, 31
4+	13, 29	3, 12
Flight time (block hrs/yr; mean ± SD)[4]	622.1 ± 252.8	31.1 ± 0.4

[1] The median number of cigarettes reported among smokers was 12 cigarettes/day.
[2] Cotinine levels were adjusted for creatinine (mg).
[3] Percentages do not equal 100 due to rounding.
[4] Source for the teachers average comes from the baseline interview and is estimated from six months prior to the study period; source for the flight attendants average comes from work history and is estimated from the four months during the study period.

DIARY RESULTS were less precise but consistent with actigraphy. FAs appear to sleep longer than teachers, but FA self-reported deep sleep and sleep quality are poorer than teachers'.

DIARY RESULTS	Flight Attendants (mean ± SD)	Teachers (mean ± SD)	P (t)
TSTMSP, hrs	8.2 ± 0.9	7.4 ± 0.8	0.001
Latency, min	12.7 ± 9.2	12.4 ± 8.4	0.87
WASO, min	16.9 ± 12.4	16.7 ± 11.0	0.95
WASO episodes	1.3 ± 1.0	1.0 ± 0.7	0.26
Deep sleep (5=very deep)	3.6 ± 0.6	3.9 ± 0.5	0.06
Sleep quality (5=very good)	3.5 ± 0.6	3.8 ± 0.5	0.04
Mood (5=very calm)	3.6 ± 0.6	3.7 ± 0.6	0.55
Feelings at wakeup (5=very alert)	3.2 ± 0.6	3.3 ± 0.6	0.54



Results: picture of actigraph data and interpretation. Please note that graphic looks different (sleep at 5 PM) in color presentation.

Results: main study findings table

① Adjusted for body mass index and decision latitude.
② Adjusted for shared home responsibilities, decision latitude, and time to take it easy while at work.
③ Adjusted for body mass index; effect factor modification with body mass index (BMI<22.91).
④ Adjusted for body mass index, hostile home environment, race, body image, and decision latitude; body mass index is an effect modifier (BMI<23.91).
⑤ Adjusted for education and job strain.
⑥ Adjusted for job strain.
⑦ Adjusted for body mass index; effect modification with body mass index (BMI<23.71).
⑧ Adjusted for body mass index and job strain; effect modification with body mass index (BMI<23.71).
⑨ Proportion of time spent sleeping in the Main Sleep Period.
⑩ Adjusted for body mass index and job strain.
⑪ Proportion of time spent sleeping in the Standard Sleep Interval from 10:00pm to 8:00am.
⑫ Adjusted for decision latitude.

①Conclusions

①This feasibility study suggests that flight attendants, on average, sleep longer than teachers. However, two actigraph indices of sleep disturbance indicated that flight attendants incurred significant impairment of sleep compared to teachers.

① In this study, actigraphy was a feasible field method for characterization of sleep disturbance in a mobile workforce, despite instrumentation problems.

① Although actigraphy is preferable to a sleep diary for field studies, the findings of this study are reflected in both unadjusted diary and adjusted actigraphy data.

① Sleep disturbance may be an indicator or component of circadian rhythm disruption. We plan to use the information from this work to inform our exposure assessment of circadian rhythm disruption in flight attendants.

Slides from ICOH presentation 9/11-14/2002 Barcelona, Spain

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Air Cabin Exposures

- Primary: Cosmic Radiation
  Circadian Rhythm Disruption
- Secondary: Tobacco smoke
  Ergonomic exposures
  Stress

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NIOSH Studies of Cabin Air Crew

Reproductive Health Studies
- Menstrual Function
- Reproductive History
- Exposure Assessment

Cancer Incidence & Mortality

Cosmic Radiation Biomarkers

Ventilation Studies
Respiratory Symptomatology

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Background

- Flight attendants may experience increased risk of:
  - Miscarriage
  - Menstrual disorders
  - Other adverse reproductive outcomes
- Is work as a female flight attendant associated with adverse reproductive effects?

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Biomonitoring Feasibility Study of Menstrual Function

- Characterize menstrual function in flight attendants and teachers (comparison group)
- Are larger studies with collection of daily urine and saliva samples feasible in a highly mobile working population?

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Air Cabin Exposures

- Primary: Cosmic Radiation
  Circadian Rhythm Disruption
- Secondary: Tobacco smoke
  Ergonomic exposures
  Stress

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Assessing Circadian Rhythm Disruption

- Travel through multiple time zones:
  - ✈External desynchronization
  - ✈Internal desynchronization
  - ✈Physiologic/behavioral disturbances including sleep-wake disturbance

NIOSH Approach

- Monitor sleep and a circadian marker
- Identify useful metrics for larger studies

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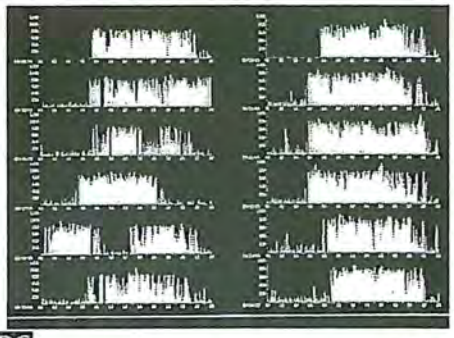

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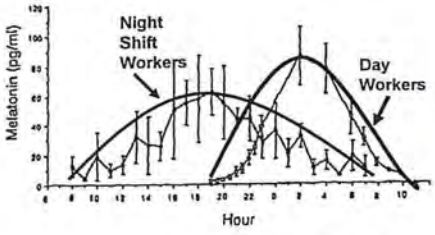

Sack et al., Sleep 15(5), 1992

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Objectives

- Determine if flight attendants are at higher risk of circadian disruption compared to teachers, as measured by melatonin production
- Identify the best metrics of circadian rhythm disruption for studies in which biomonitoring is infeasible

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Methods

- 45 flight attendants, 26 teachers
- For one menstrual cycle:
  - Collected/ measured overnight urine
  - Daily diary
  - Activity monitor
- 6-sulfatoxymelatonin measured by RIA
- Individual flight history records

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Covariates

- Demographics, BMI
- Medications, stress, exercise
- Urinary cotinine
- Lifestyle and stress

Measures of Melatonin

- Overnight melatonin production rate
- Within-woman variance of overnight rate
- % low melatonin days (within-woman)

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Methods--analysis

- Linear and multiple logistic regression
  - Adjusted means, odds of high or low quartile
- Linear mixed-effects model
  - Adjusted daily melatonin rates
  - Within-woman variance estimates
- Factor analysis
  - Simplify 16 measures of sleep, activity, melatonin, and flight history

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Results: Melatonin Rate

Melatonin rate (ng/kg/h)	Crude mean	Crude OR	Adjusted mean, Mixed Model
Flight Attendants	[illegible]	[illegible]	[illegible]
Teachers	[illegible]	1.0	[illegible]

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Results: Melatonin Variance

Variance ($\times 10^{-5}$ (ng/h)^2)	Crude mean	Adjusted mean	Crude OR	Adjusted OR
Flight Attendants	2.4 (1.6 – 3.4)	2.4 (1.8 – 3.6)	2.2 (0.6 – 7.9)	2.3 (0.6 – 9.1)
Teachers	1.3 (0.8 – 2.1)	1.0 (0.5 – 1.9)	1.0	1.0

Mixed Model	Within-Woman Variance	Between-Woman Variance
Flight Attendants	4.3 (4.0 – 4.6)	2.7 (1.4 – 4.1)
Teachers	2.6 (2.4 – 2.9)	5.0 (2.0 – 8.1)

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Factor analysis

- Simplify 16 measures of sleep, activity, melatonin, and flight history
- How do these measures describe circadian disruption?
- Which measures are the best metrics for a large study without melatonin biomonitoring?

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- Melatonin (N=5)
- Sleep displacement/activity (N=7)
- Flight history data (N=4)

FACTOR ANALYSIS

3 Factors Describe Circadian Disruption

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3 Factors Describe Circadian Disruption

1. Sleep, Work, Time Zones (52.8%)
2. Melatonin, Time Zones (13.5%)
3. Melatonin and Sleep Efficiency (9.1%)

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Conclusions: Circadian Disruption

- Flight attendants experience increased circadian rhythm disruption, as measured by more variable melatonin rates.

- For studies without biomonitoring, time zones crossed is a useful indicator of both sleep displacement and melatonin desynchronization.

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" ...the 1990 direct cost of sleep disorders and deprivation may be as much as 15.9 billion dollars." (National US Commission on Sleep Disorders Research)

indirect and related costs from sleep disorders/deprivation resulting in stress-related, reduced workplace productivity: $150 billion (United States)

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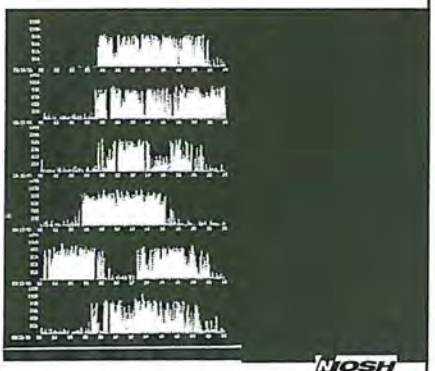

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