Sleep, performance, circadian rhythms, and light-dark cycles during two space shuttle flights

DERK-JAN DIJK,1 DAVID F. NERI,1,2 JAMES K. WYATT,1 JOSEPH M. RONDA,1 EYMARD RIEL,1 ANGELA RITZ-DE CECCO,1 ROD J. HUGHES,1 ANN R. ELLIOTT,3 G. KIM PRISK,3 JOHN B. WEST,3 AND CHARLES A. CZEISLER1

1Division of Sleep Medicine, Department of Medicine, Brigham and Women’s Hospital, Harvard Medical School, Boston, Massachusetts 02115; 2Fatigue Countermeasures Program, National Aeronautics and Space Administration Ames Research Center, Moffett Field 94035; and 3Department of Medicine, University of California, San Diego, La Jolla, California 92093

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Address for reprint requests and other correspondence: D.-J. Dijk, Centre for Chronobiology, School of Biomedical and Life Sciences, Univ. of Surrey, Guildford GU2 7XH, UK (E-mail: d.j.dijk@surrey.ac.uk).

HUMAN SLEEP and circadian rhythms have evolved in adaptation to an environment characterized by a 24-h light-dark cycle and a gravitational force of 1 G. During spaceflight, both the exposure to the main synchronizer of the human circadian timing system, i.e., the light-dark cycle, as well as exposure to gravitational forces are altered dramatically. The potential impact of these changes on sleep-wake patterns, circadian rhythms, and performance was recognized shortly after the advent of manned spaceflight (2, 32). Polysomnographic recordings of sleep and assessment of subjective sleep quality during Skylab missions (15, 16), space shuttle missions (30, 36), and Mir missions (20–22) have documented that, on average, sleep is of shorter duration in space. In addition, some of these reports, but not all, indicate changes in sleep structure and changes in circadian phase and amplitude. The mechanisms underlying this sleep reduction during space missions have not been elucidated. Factors such as space adaptation syndrome, excitement, workload, adaptation to weightlessness itself, and changes in light-dark cycles may all play a role (37). Furthermore, before, during, and after spaceflight the sleep-wake schedules of astronauts are affected by social and operational demands as well as by adaptation to local time zones immediately before and after missions. These demands often require complex rest-activity cycles that potentially jeopardize optimal alignment of the sleep-wake cycle and the circadian timing system and thereby induce sleep loss, buildup of homeostatic sleep pressure, and associated decrements in daytime alertness and performance.

The National Aeronautics and Space Administration (NASA) has recognized the importance of adequate sleep duration and circadian rhythm alignment and, for the shuttle program, has implemented preflight circadian adaptation countermeasures, as well as in-flight sleep-wake schedules to optimize circadian adaptation and to minimize sleep loss. In particular, for missions that require shifted wake times on the day of launch and, consequently, shifted wake times on the subsequent in-flight days, astronauts are exposed to a light-dark regime before launch to shift their circadian system to the required phase (6, 41). Landing considerations often require that in the course of a shuttle mission, sleep-wake cycles are advanced by approximately 4 to 5 h relative to the time of launch. In an
attempt to minimize circadian disruption and to maintain synchrony between the circadian timing system and the rest-activity cycle, this advance is achieved by either identical daily shifts of 20–40 min or a smaller number of incremental shifts not to exceed 2 h on any given flight day.

Despite these attempts to optimize sleep-wake schedules, and even though astronauts are scheduled to sleep for 8 h every mission night, survey data as well as polysomnographic recordings indicate that sleep duration is reduced to approximately 6–6.5 h/day during shuttle missions (30, 36). The sleep problems during spaceflight are so pervasive that hypnotics (benzodiazepine and non-benzodiazepine allosteric modulators of the benzodiazepine-γ-aminobutyric acid receptor complex) are the second most commonly used medications during space shuttle missions (33).

From a circadian perspective this sleep reduction may be related to the average imposed period (23.33–23.66 h) of the scheduled rest-activity cycle on most U.S. space shuttle flights. This period is more than 0.5 h shorter than the 24.18-h intrinsic period of the human circadian pacemaker assessed under laboratory forced desynchrony conditions (7) and the 24.35-h period observed in submariners scheduled to an 18-h rest-activity cycle during a voyage on a submarine (24). Failure of the circadian pacemaker to advance at a rate comparable to that of the scheduled sleep-wake cycle would be reflected in an apparent delay of endogenous rhythms relative to the advanced timing of the scheduled sleep-wake cycle.

Such a phase advance of the scheduled sleep episode relative to the endogenous circadian rhythms could result in a scheduled bedtime that coincides with the wake maintenance zone (8, 40), which is located just before the onset of nocturnal melatonin secretion (27). Model simulations (1) and laboratory studies in which the sleep-wake cycle was desynchronized from endogenous circadian rhythms indicate that such scenarios could very well lead to sleep disruption and neurobehavioral performance deficits (9, 43).

To further investigate these issues, we documented the illumination levels, as well as rest-activity cycles shorter than 24 h, during spaceflight. We quantified the effects of spaceflight on sleep duration and sleep structure, circadian rhythms, and neurobehavioral performance. In addition, we assessed the efficacy of melatonin (0.3 mg) as a countermeasure for sleep disturbances during shuttle missions STS-90 (Neurolab) and STS-95 in a double-blind placebo-controlled crossover design. In view of melatonin’s putative role in silencing the circadian wake-promoting signal (27, 35), which peaks at the end of the habitual waking day and is generated by the circadian pacemaker (8, 26), it appeared rational to use melatonin as a hypnotic on a phase-advancing sleep-wake cycle, such as that implemented during shuttle missions.

METHODS

Subjects

Five astronauts, one woman and four men (age 37–46 yr), participated in these studies. Four participated in the 16-day STS-90 mission devoted to the neurosciences (Neurolab: April 17–May 03, 1998), and one served as a payload specialist on the 10-day STS-95 mission (October 29–November 7, 1998). Three of these participants underwent a clinical polysomnographic (PSG) recording for sleep disorders evaluation. These clinical recordings were repeated in two of these three individuals. They all met NASA health criteria for flight assignment. Before the mission the astronauts were trained extensively in application of sensors, operation of the equipment, and recognition of the quality of electroencephalogram (EEG), electrooculogram (EOG), electrocardiogram (ECG), and electromyogram (EMG) signals and also performed several training sessions on the neurobehavioral performance battery. During the missions the astronauts conducted and participated in a variety of experiments. The sleep experiment was approved by the Human Research Committee of the Brigham and Women’s Hospital and the NASA-Johnson Space Center (JSC) Institutional Review Board. Before the beginning of the study, each subject gave written informed consent.

Actigraphy

To assess sleep duration unobtrusively, actigraphic recordings were obtained continuously during the two missions, as well as during several segments before and immediately after the missions. The Mini Motionlogger actigraph (Ambulatory Monitoring, Ardsley, NY) was worn on the nondominant wrist. During preflight and postflight recordings, actigraphs were initialized and then given to the crew before each data collection segment. The battery life and memory of the actigraphs are limited, and therefore actigraphs were exchanged in the middle of the 16-day STS-90 mission. Before flight, these units were preinitialized and the timer was set to automatically activate the units at specific times. Actigraphy data were analyzed with the ACTION-W software program (version 1.06; Ambulatory Monitoring). To assess total sleep time during scheduled sleep episodes, an established algorithm was used (5). Start and end of each sleep episode was determined on the basis of an internal event marker pressed by the wearer and examination of the actigraph data.

Polysomnography

Sleep net. Sleep was recorded using a sensor array (e-Net Physiomex, North Billerica, MA). The sleep cap, hereinafter referred to as the sleep net, is an integrated set of components consisting of a reusable customized headpiece and disposable silver/silver chloride hydrogel biosensors (Hydrodot Biosensors, Physiomex). Electrodes were positioned in sockets according to the International 10–20 System: two mastoid reference electrodes, one forehead ground electrode, two EOG electrodes, four EEG electrodes (C3, C4, O1, O2), and four chin EMG electrodes. The shielded wire leads on the outside of the sleep net were combined into a single connector that attached to the outside of the sleep reader (DSR) via a single connector.

DSR. All PSG recordings were acquired on a modified Vitasport-2 DSR (Temec Instruments, Kerkrade, The Netherlands), a portable, modular battery-operated PSG recorder with a 12-bit analog-to-digital converter. For the present
purposes, 20 channels were used to record and store EEG, EOG, and EMG signals, as well as signals from a breathing sound microphone, a light sensor, two respiratory inductance plethysmograph channels, a nasal/oral airflow thermistor, a finger-pulse oximeter, and a two-lead ECG to analyze breathing parameters during sleep (14). For this report, we analyzed EEG, EOG, and EMG data. EEGs were low pass filtered at 70 Hz and high pass filtered with a time constant of 0.33 s, sampled at 256 Hz, and stored at 128 Hz. EOG signals were low pass filtered at 35 Hz, high pass filtered with a time constant of 1 s, sampled at 128 or 256 Hz, preprocessed with a moving average filter, and stored at 64 Hz. EMG signals were low pass filtered at 100 Hz and high pass filtered with a time constant of 0.015 s and sampled at 128 or 256 Hz and stored at 128 Hz.

The data collected on the DSR were stored on PCMCIA 84 MB Flash Ram cards (SanDisk, Sunnyvale, CA). During the STS-90 mission, data were transferred to a microcomputer and downlinked, allowing inspection of the data by the investigators after each in-flight sleep recording.

Sensor impedances were checked using a NASA-customized impedance meter or a GRASS EZM4 impedance meter. During and after instrumentation, but before sleep, all physiological signals were displayed in real time, on the screen of a laptop using an expert system for astronaut assistance (4). This allowed inspection of signal quality before the sleep recordings. In flight the astronauts were scheduled to sleep in the dedicated individual sleep compartments, which provided some shielding from noise and light. One astronaut reported that he slept in these compartments only on the four nights during which PSG recordings were obtained because it was being used by the Commander on the non-PSG nights.

For all analyses presented here, PSG recordings were scored according to standard criteria (34) by E. Riel, whose scoring was validated against two PSG recordings of each astronaut scored jointly by D.-J. Dijk, J. K. Wyatt, and R. J. Hughes. Manual scores were transferred to the laboratory database and further analyzed by software written in Turbo Pascal and SAS statistical software (SAS Institute, Cary, NC).

For the PSG recordings, total dark time (TDT) was determined from the light sensor signal and provided a reference for the analysis. Sleep latency was defined as the interval between lights out and the first epoch of sleep. Latency to rapid eye movement (REM) sleep was defined as the interval between sleep onset and the first epoch of REM sleep.

Subjective Sleep Quality

After each sleep episode, astronauts completed a computerized subjective sleep quality questionnaire or a paper equivalent. This questionnaire assessed sleep latency, sleep duration, and sleep quality, as well as causes of sleep disruption and use of medication.

Neurobehavioral Assessment

Neurobehavioral assessments (duration ~23 min) were obtained in the afternoons after the nights of PSG recordings. The assessment battery included a 10-min psychomotor vigilance task (PVT) (13). The PVT is a high-signal-load reaction time task with feedback that has been used to measure sustained attention and reaction time in many operational environments. A 4-min two-digit addition task (ADD) served as a measure of cognitive throughput. The probed recall memory task (PRM) (11), with 10 min between the 30-s presentation of six word pairs and 1 min of probed recall, served as a measure of memory. The 30-s performance, effort, and evaluation rating scale (PEERS; Ref. 12) allowed for a subjective assessment of performance and effort. A collection of visual analog scales (VAS; 2 min) and the Karolinska sleepiness scale (KSS) (3) measured various aspects of mood as well as sleepiness. The assessment battery also included a 3-min psychomotor tracking task (not reported here). These tasks have been shown to be sensitive to circadian phase misalignment and the duration of wakefulness (43). This neurobehavioral battery was administered on an IBM Thinkpad (in flight) or a comparable laptop computer (preflight and postflight).

Body Temperature Recordings

Core body temperature was recorded with a body core temperature monitoring system (BCTMS). The BCTMS consists of a radio-frequency receiver (Personal Electronics Devices, Wellesley, MA) used in combination with an ingestible temperature sensor (CorTemp 100 sensor, HTI Technologies, St. Petersburg, FL). Data were stored every 15 s. BCTMS recorders were initialized and downloaded by software written by J. M. Ronda through an interface box connected to the Thinkpad.

Body temperature data were visually inspected, and artifacts were removed. Average curves were computed by aligning data to estimated onset of sleep and plotted against the average timing of sleep onset. Amplitude and phase, as well as their asymptotic SEs and 95% confidence intervals (CI) of the averaged curves, were computed by fitting a sine wave to the data using nonlinear regression (SAS). The period of the sine wave was allowed to vary between 1,420 and 1,460 min.

Urine Collection and Hormonal Measures

Urine was collected during preflight, in-flight, and postflight segments. All voids during selected 24-h episodes were collected in containers: lithium chloride was added to the containers used in flight. During the preflight and postflight segments, samples were stored on ice, whereas during flight the voids were frozen at -20°C until further processing.

Total urine volume was determined for the preflight and postflight segments by measuring the volume. For in-flight samples, volume was determined on the basis of the lithium chloride concentration by the JSC Clinical Laboratory. Urine was assayed for urinary free cortisol using radioimmunoassay (assay sensitivity 0.3 µg/ml, intra-assay coefficient of variation 4.5%, interassay coefficient of variation 6.2%) at the Core Laboratory of the General Clinical Research Center at Brigham & Women's Hospital.

Urine samples were also assayed for 6-sulfatoxymelatonin by radioimmunoassay (assay sensitivity of 1 ng/ml; intra- and interassay coefficients of variation were 5.4 and 8.7%, respectively; DiagnosTech, Osceola, WI). Cortisol time series were constructed by computing cortisol secretion per minute for every minute of the interval between consecutive voids. These individual time series were then averaged across subjects.

Illuminance

Actillumes (Ambulatory Monitoring, Ardsley, NY) were used as light measurement devices. They were equipped with an external battery pack to allow for continuous recordings of illuminance during the entire mission with a storage frequency of 1 sample/min. Initialization and downloading of the actillumes were performed on the ground preflight and postflight, respectively. The actillumes, as well as all other monitoring devices, were synchronized to GMT and activated...
shortly before launch. Illuminances were recorded continu-
ously in the three habitable compartments of the space
shuttle. During the STS-90 mission, actillumes were placed on
the flight deck, in the windowless middeck, and in the
Spacelab. During the STS-95 mission, actillumes were placed
on the flight deck, in the windowless middeck, and in the
Spacehab, which is equipped with small portholes.

Illuminance data were analyzed by computing the time
course during scheduled sleep and wake episodes and the
distribution of these values. Both arithmetic and geometric
means were computed because the distribution of lux values
is not normal and the relationship between illuminance and
circadian phase shifting is nonlinear (44). The geometric
means better reflect the drive of environmental light onto
the circadian pacemaker.

Melatonin Administration
Hypnotic effects of melatonin have been reported for a
wide dose range, although the optimal doses for such effects
have not been firmly established (35, 39). A 0.3-mg dose of
melatonin was selected because in a laboratory study we
found that a 0.3-mg dose significantly improved sleep at
adverse circadian phases, including the wake maintenance
zone (42), and that plasma melatonin concentrations had
returned to baseline at the end of sleep episodes. As part of
an FDA-approved phase II clinical trial, melatonin or placebo
was taken 30 min before scheduled bedtime for preflight
segments 2 mo (L-60 day) and 1 mo (L-30 day) before launch
and scheduled to be taken 30 min before all sleep episodes
during the in-flight segment. Administration occurred in a
double-blind balanced manner such that melatonin and pla-
CEO were administered on alternate nights. Melatonin was
manufactured (Regis Chemical, Morton Grove, IL) and
placed into gelatin capsules with cellulose as the vehicle by
the Investigational Drug Service of the Brigham and
Women’s Hospital. Purity and stability testing was per-
formed by an independent laboratory (Chemir/Polytech,
Maryland Heights, MO) on capsules of this lot.

Astronauts reported the use of medication in the comput-
erized sleep log. Use of zolpidem (Ambien) was reported in
one case during a sleep episode when no PSG recording was
made.

Preflight Baseline Assessments
Preflight assessments of sleep, neurobehavioral perfor-
mance, and hormonal measures occurred approximately 3, 2,
and 1 mo before flight in astronaut crew quarters at JSC
(STS-90) or at a local inn (STS-95). The data-acquisition
segment 3 mo before the mission was considered an adapta-
tion to recording procedures and equipment segment, and
these data were not included in the current analyses.

Seven days before scheduled launch, the NASA preflight
quarantine protocol began. As part of that protocol, crew-
members slept in crew quarters and had reduced social and
family contact. Three days before scheduled launch they were
transferred to the Kennedy Space Center (KSC) in Florida.
During each of the baseline segments, actigraphy was con-
ducted for at least 48 consecutive hours, including two nights
during which PSG recordings were obtained. In addition,
subjective sleep quality was assessed on awakening in the
morning. In the afternoons after the PSG recordings, subjects
conducted a neurobehavioral performance test. Urine was
collected for 24 h, starting upon awakening after the first
PSG recording. Body temperature was recorded for >32 h
starting on the evening of the first PSG recording and con-
tinuing through the second night of PSG recording. STS-90
subjects were scheduled to sleep in individual bedrooms from
2300 to 0700. STS-95 subjects were scheduled to sleep from
2300 to 0700 on L-60 and from 2230 to 0630 on L-30 and
L-15. For the STS-90 mission additional baseline data were
collected during the quarantine before launch. Sleep was
recorded for three consecutive sleep episodes, and actigraphy,
neurobehavioral function, and subjective sleep quality
were recorded throughout the quarantine period until
launch. For STS-95 no PSG recordings were obtained during
the quarantine period, but actigraphy, neurobehavioral func-
tions, and sleep logs were collected.

The crew of both flights were stationed at JSC and lived on
the local time zone (Central Daylight Time, i.e., 5 h later than
GMT). Three days before scheduled launch (i.e., 4 days before
actual launch of STS-90), they left for the KSC in Florida
(Eastern Time Zone).

Launch occurred at 1419 (Eastern Daylight Time; EDT) for
STS-90 and 1420 (Eastern Standard Time; EST) for STS-95.
This corresponds to 1819 and 1920 GMT for STS-90 and
STS-95, respectively. Awakening on the day of launch oc-
curred ~7 h before launch, and the first 8-h sleep episode
was scheduled to start at 0459 (GMT) for STS-90 and 0545 (GMT)
for STS-95. The scheduled 8-h sleep episodes during the in-
flight segment advanced ~20 min each day on STS-90 and
35 min each day on STS-95. A raster plot of the scheduled
sleep-wake cycles for STS-90 is provided in Fig. 1. All times
are in GMT to allow for data alignment across measures and
time zones. Pooling of data collected during the two missions
was performed by subdividing the missions into segments
(preflight, early flight, etc.).

In-Flight Data Acquisition
Astronauts wore actigraphs on their nondominant wrist
together throughout the missions, except for short episodes during
which time-specific operational demands or scientific exper-
iments precluded this. Every morning on awakening, astro-
naughts completed the computerized sleep log (STS-90) or pa-
per equivalent (STS-95).

PSG recordings were made early and late in flight. On
STS-90, subjects were divided in two groups, and the PSG
recordings were staggered such that group A conducted PSG
recordings on flight day (FD) 3 and FD4 (early flight) and on
FD12 and FD13 (late flight), and group B conducted the
recordings on FD5 and FD6 (early flight) and on FD14 and
FD15 (late flight). On STS-95 sleep recording were made on
FD4 and FD5 (early flight) and on FD7 and FD8 (late flight).

In the afternoon after the instrumented sleep recordings,
subjects conducted the neurobehavioral assessment battery.
On STS-90, body temperature was recorded during two
~40-h sessions, starting on FD5 and FD14. On STS-95, body
temperature was recorded continuously from FD2 to FD9
(data not included). The 24-h episodes of urine collection
began with the first void of the day on FD6 and FD15 on
STS-90 and on FD3 and FD6 for STS-95.

Postflight Recording Schedules
Actigraphic recordings were resumed shortly after land-
ing. The first night after landing was spent at KSC, and
astronauts flew to JSC the following day. PSG recordings
were obtained during the first, third, and fourth night at
JSC. This corresponds to the second, fourth, and fifth sleep
episode after landing. Neurobehavioral performance was
assessed during the afternoon after the PSG recordings. Urine
was collected for a 24-h episode starting before the first sleep
episode at JSC.
For the STS-95 mission, urine was not collected during the postflight segment.

Statistics

Subjective sleep quality data, PSG data, actigraphy data, and neurobehavioral performance data were analyzed with repeated-measures ANOVA when possible. In this ANOVA the factor mission segment had three levels (preflight, in flight, postflight). For each subject a mean was computed for each level (i.e., segment of the mission) and entered into the ANOVA. Statistical analyses of the detailed time course of neurobehavioral performance for which missing data precluded use of repeated-measures ANOVA were performed with ANOVA on $z$-transformed data. Effects of melatonin were assessed for the flight segment of the experiment, and these effects were analyzed for the first and second half of the mission separately. The time course of selected PSG variables was analyzed with two-factor ANOVAs with repeated measures. In cases for which the ANOVA was significant, paired Student’s $t$-tests were used for post hoc comparisons. Effect sizes were computed for in-flight vs. preflight comparisons, as well as for postflight vs. preflight comparisons of actigraphy, subjective sleep quality, polysomnographically recorded sleep, mood, and neurobehavioral performance. Effect sizes were computed as the difference between the means divided by the standard deviation. The standard deviation was determined using the pooled variance of the two samples. All means represent averages across subjects, and $n = 5$ unless indicated otherwise. Standard errors are the measure of variability, unless indicated otherwise.

RESULTS

Rest-Activity Cycles and Actigraphy

Actigraphy revealed a number of salient features of the rest-activity cycles of astronauts (Fig. 2). The preflight rest-activity cycle was characterized by a 24-h periodicity and a phase advance of $\approx 1$ h, which was especially apparent for the onset of activity, associated with the travel from JSC to KSC. The in-flight actigraphy clearly demonstrated the progressive phase advance of wake time associated with the imposed shorter than 24-h sleep-wake schedule, and the deviation from this schedule on FD8 due to operational reasons. In this subject it appears that the day-to-day variability in the onset of activity (wake time) is much smaller than the day-to-day variability in offset of activity before (L-), during (FD), and after (R) the STS-90 (Neurolab) mission. FDs are numbered such that FD1 starts at launch and ends at the end of the 1st in-flight sleep episode. Scheduled polysomnographic recordings (open horizontal bars), neurobehavioral performance tests (open triangles), urine collection sessions (stippled horizontal lines), body temperature recordings (solid horizontal line), and placebo (○), and melatonin (●) administration are indicated for treatment group B (see METHODS for a description of differences between groups A and B). Time of day is indicated as Central Daylight Time (CDT; top horizontal axis) and Greenwich Mean Time (GMT; bottom horizontal axis).

For the STS-95 mission, urine was not collected during the postflight segment.

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activity (bedtime). The postflight segment illustrates the abrupt ~4-h phase delay of the rest-activity cycle. The pattern displayed is typical of the other subjects.

**Effects of spaceflight.** Sleep period time (SPT, defined as the first interval in minutes between the first and last epochs of sleep) and total sleep time (TST; SPT minus wakefulness during the sleep period) were estimated from the actigraphic recordings for the preflight, in-flight, and postflight segments separately, as well as separated by drug condition. SPT varied significantly over the three global segments such that in the placebo condition SPT in flight was significantly shorter than during postflight and tended to be shorter \(P = 0.0606\) compared with preflight (Table 1). Similar trends were observed for actigraphically assessed TST, although these effects did not reach statistical significance.

**Effects of melatonin.** No significant effects of presleep administration of this dose of melatonin were detected for any of the actigraphic measures (Table 2).

### Subjective Sleep Quality

**Effect of spaceflight.** Several aspects of subjective sleep quality, assessed on the mornings after intake of placebo, varied over the three global segments (preflight, in flight, postflight) of the experiment (Table 3). This variation was such that, in general, sleep was perceived as best on return from space and worst in space. In particular, subjective estimates of sleep latency, sleep quality, and the feeling of being physically rested on awakening all varied significantly, and all indicated best sleep after return to earth. Similar results were obtained when the placebo and melatonin data were combined (Fig. 3). A comparison of subjective sleep quality during the first and second half of the mission suggested that subjective sleep quality deteriorated in the course of the mission, but no statistically significant changes were observed.

### Table 1. Actigraphy and PSG sleep parameters preflight, in flight, and postflight

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<tr>
<th></th>
<th>Preflight</th>
<th>In Flight</th>
<th>Postflight</th>
<th>(F_{2,5} (P\text{ Value}))</th>
<th>(\text{Effect Size})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actigraphy SPT, min</td>
<td>458.2 ± 7.1</td>
<td>427.6 ± 6.8</td>
<td>462.4 ± 8.4*</td>
<td>5.41 (0.0326)</td>
<td>-2.0 (0.2)</td>
</tr>
<tr>
<td>Actigraphy TST, min</td>
<td>417.8 ± 14.1</td>
<td>396.4 ± 9.8</td>
<td>403.7 ± 21.9</td>
<td>1.21 (0.3483)</td>
<td>-0.8 (0.3)</td>
</tr>
<tr>
<td>Sleep latency, min</td>
<td>9.9 ± 2.7</td>
<td>11.1 ± 1.9</td>
<td>5.6 ± 1.4</td>
<td>1.45 (0.2948)</td>
<td>0.2 (0.9)</td>
</tr>
<tr>
<td>Total dark time, min</td>
<td>482.3 ± 6.8</td>
<td>465.3 ± 5.6</td>
<td>478.4 ± 5.4</td>
<td>1.34 (0.3147)</td>
<td>-1.0 (0.2)</td>
</tr>
<tr>
<td>TST, min</td>
<td>404.8 ± 11.8</td>
<td>391.2 ± 7.6</td>
<td>405.1 ± 22.1</td>
<td>0.40 (0.6806)</td>
<td>-0.6 (0.0)</td>
</tr>
<tr>
<td>Waking after sleep onset</td>
<td>68.3 ± 10.2</td>
<td>63.1 ± 7.9</td>
<td>67.7 ± 17.0</td>
<td>0.26 (0.7386)</td>
<td>-0.3 (0.0)</td>
</tr>
<tr>
<td><em>Stage 1</em>, min</td>
<td>60.9 ± 10.4</td>
<td>50.8 ± 7.4</td>
<td>67.7 ± 6.4</td>
<td>2.62 (0.1331)</td>
<td>-0.5 (0.3)</td>
</tr>
<tr>
<td><em>Stage 2</em>, min</td>
<td>182.9 ± 15.5</td>
<td>196.7 ± 7.3</td>
<td>178.3 ± 15.9</td>
<td>0.51 (0.6167)</td>
<td>0.5 (0.1)</td>
</tr>
<tr>
<td>Slow-wave sleep, min</td>
<td>60.7 ± 6.9</td>
<td>52.9 ± 10.7</td>
<td>39.6 ± 4.4</td>
<td>2.97 (0.1084)</td>
<td>-0.4 (1.6)</td>
</tr>
<tr>
<td>REM sleep, min</td>
<td>99.5 ± 12.3</td>
<td>90.9 ± 4.9</td>
<td>119.6 ± 13.6</td>
<td>2.99 (0.1086)</td>
<td>-0.4 (0.7)</td>
</tr>
<tr>
<td>Sleep efficiency, %</td>
<td>83.8 ± 2.1</td>
<td>84.0 ± 1.8</td>
<td>84.5 ± 4.0</td>
<td>0.08 (0.8359)</td>
<td>0.1 (0.1)</td>
</tr>
<tr>
<td><em>Stage 1</em>, %</td>
<td>15.5 ± 3.1</td>
<td>13.3 ± 1.8</td>
<td>17.4 ± 2.8</td>
<td>1.49 (0.2812)</td>
<td>-0.4 (0.3)</td>
</tr>
<tr>
<td><em>Stage 2</em>, %</td>
<td>45.2 ± 3.6</td>
<td>50.1 ± 2.0</td>
<td>43.6 ± 2.3</td>
<td>1.89 (0.2124)</td>
<td>0.8 (0.2)</td>
</tr>
<tr>
<td>Slow-wave sleep, %</td>
<td>15.0 ± 1.5</td>
<td>13.7 ± 2.8</td>
<td>10.0 ± 1.0</td>
<td>2.18 (0.1828)</td>
<td>-0.2 (-1.7)</td>
</tr>
<tr>
<td>REM sleep, %</td>
<td>24.4 ± 2.6</td>
<td>22.9 ± 1.5</td>
<td>29.0 ± 1.9</td>
<td>3.31 (0.1188)</td>
<td>-0.3 (0.9)</td>
</tr>
<tr>
<td>Latency to REM, min</td>
<td>86.4 ± 13.1</td>
<td>74.3 ± 3.9†</td>
<td>43.3 ± 2.5§</td>
<td>9.7 (0.0269)</td>
<td>-0.6 (-2.0)</td>
</tr>
</tbody>
</table>

Preflight, in-flight, and postflight values are means ± SE; \(n = 5\) subjects. Only data obtained after intake of placebo are included in analysis. \(F\) values represent the \(F\) values for the factor segment (preflight, in flight, or postflight) derived from a repeated-measures ANOVA. Paired \(t\)-tests were used for pairwise comparisons if ANOVA was significant. Significant differences: \(*\) in flight vs. postflight, \(P < 0.05\); \(†\) in flight vs. preflight, \(P < 0.05\); \(§\) postflight vs. preflight, \(P < 0.05\). Variable names with actigraphy were derived from actigraphy; all other variables were derived from polysomnography (PSG). SPT, sleep period time; TST, total sleep time; REM, rapid eye movement.

### Table 2. Effects of melatonin on actigraphic and PSG sleep parameters preflight and in flight

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Melatonin</th>
<th>Placebo</th>
<th>Melatonin</th>
<th>Melatonin (F_{1,4}) ((P = ))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actigraphic SPT, min</td>
<td>460.2 ± 12.1</td>
<td>473.1 ± 3.2</td>
<td>427.6 ± 6.8</td>
<td>426.3 ± 5.3</td>
<td>0.54 (0.5040)</td>
</tr>
<tr>
<td>Actigraphic TST, min</td>
<td>414.8 ± 21.6</td>
<td>414.5 ± 14.2</td>
<td>396.4 ± 9.8</td>
<td>386.7 ± 13.8</td>
<td>0.54 (0.5019)</td>
</tr>
<tr>
<td>Sleep latency, min</td>
<td>13.4 ± 2.6</td>
<td>6.4 ± 0.4*</td>
<td>11.1 ± 1.9</td>
<td>9.6 ± 1.3</td>
<td>75.96 (0.0010)</td>
</tr>
<tr>
<td>TST, min</td>
<td>400.5 ± 8.1</td>
<td>417.6 ± 8.5</td>
<td>391.2 ± 7.6</td>
<td>376.1 ± 5.5</td>
<td>0.04 (0.8502)</td>
</tr>
<tr>
<td>Sleep efficiency, %</td>
<td>82.3 ± 0.9</td>
<td>86.4 ± 2.0</td>
<td>84.0 ± 1.8</td>
<td>82.3 ± 1.6</td>
<td>0.72 (0.4345)</td>
</tr>
<tr>
<td><em>Stage 1</em>, %</td>
<td>16.1 ± 3.2</td>
<td>17.1 ± 1.7</td>
<td>13.3 ± 1.8</td>
<td>13.9 ± 1.9</td>
<td>0.43 (0.5457)</td>
</tr>
<tr>
<td><em>Stage 2</em>, %</td>
<td>45.4 ± 3.9</td>
<td>46.0 ± 1.8</td>
<td>50.1 ± 2.0</td>
<td>46.8 ± 3.1</td>
<td>7.18 (0.0552)</td>
</tr>
<tr>
<td>Slow-wave sleep, %</td>
<td>15.1 ± 1.0</td>
<td>13.7 ± 1.1</td>
<td>13.7 ± 2.8</td>
<td>15.4 ± 1.5</td>
<td>0.01 (0.9297)</td>
</tr>
<tr>
<td>REM, %</td>
<td>23.3 ± 1.9</td>
<td>23.3 ± 0.8</td>
<td>22.9 ± 1.5</td>
<td>23.9 ± 1.9</td>
<td>2.32 (0.2025)</td>
</tr>
<tr>
<td>REM latency, min</td>
<td>76.3 ± 2.0</td>
<td>65.7 ± 7.1</td>
<td>74.3 ± 3.9</td>
<td>70.6 ± 3.1</td>
<td>2.07 (0.2235)</td>
</tr>
</tbody>
</table>

Preflight and in-flight values are means ± SEs; \(n = 5\) subjects. Melatonin \(F_{1,4}\) represents the \(F\) values for the factor melatonin as obtained in a 2-factor ANOVA for repeated measures. Paired \(t\)-tests were used for pairwise comparisons. Significant difference: \(^*\) Preflight melatonin vs. preflight placebo, \(P < 0.05\).
Effect of melatonin. Subjective sleep quality after melatonin administration was compared with placebo for the preflight segment (L-60 and L-30) and the in-flight segment by a two-factor ANOVA for repeated measures. A significant effect of melatonin was observed only for the number of awakenings ($F_{1,14} = 11.43; P = 0.0278$). The number of reported awakenings was higher after melatonin administration, although post hoc comparisons for the preflight and in-flight segment separately did not reveal significant differences between the placebo and melatonin condition ($P > 0.1$). Significant effects of melatonin were not observed for any of the other variables, and none of the pairwise comparisons between placebo and melatonin for the preflight and in-flight segment approached significance (data not shown).

**Table 3. Subjective sleep quality preflight, in flight, and postflight**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Preflight</th>
<th>In Flight</th>
<th>Postflight</th>
<th>$F_{2,8}$ ($P$-value)</th>
<th>Effect Size Preflight vs. Postflight</th>
<th>Effect Size Postflight vs. Preflight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep latency, min</td>
<td>22.0 ± 6.6</td>
<td>27.6 ± 6.6</td>
<td>14.6 ± 3.9†</td>
<td>7.30 (0.0157)</td>
<td>0.4</td>
<td>-0.6</td>
</tr>
<tr>
<td>TST, min</td>
<td>409 ± 9</td>
<td>390 ± 15</td>
<td>429 ± 18</td>
<td>3.72 (0.0719)</td>
<td>-0.7</td>
<td>0.6</td>
</tr>
<tr>
<td>Sleep quality (1–9)</td>
<td>6.5 ± 0.3</td>
<td>5.4 ± 0.4§</td>
<td>6.8 ± 0.3‡</td>
<td>10.26 (0.0207)</td>
<td>-1.3</td>
<td>0.5</td>
</tr>
<tr>
<td>Sleep maintenance (1–9)</td>
<td>6.4 ± 0.4</td>
<td>5.4 ± 0.6</td>
<td>6.4 ± 0.4</td>
<td>3.68 (0.1099)</td>
<td>-0.9</td>
<td>0.0</td>
</tr>
<tr>
<td>Physically rested (1–9)</td>
<td>6.3 ± 0.5</td>
<td>5.4 ± 0.4§</td>
<td>6.6 ± 0.3‡</td>
<td>13.57 (0.0027)</td>
<td>-0.9</td>
<td>0.3</td>
</tr>
<tr>
<td>Mentally alert (1–9)</td>
<td>6.4 ± 0.6</td>
<td>5.7 ± 0.5</td>
<td>6.4 ± 0.2</td>
<td>1.84 (0.2196)</td>
<td>-0.5</td>
<td>0.0</td>
</tr>
<tr>
<td>Awakenings, number</td>
<td>1.0 ± 0.1</td>
<td>1.5 ± 0.4</td>
<td>1.2 ± 0.2</td>
<td>1.22 (0.3325)</td>
<td>0.8</td>
<td>0.7</td>
</tr>
<tr>
<td>Compared with earth, (1–9)</td>
<td>4.6 ± 0.8</td>
<td>4.9 ± 0.6</td>
<td>5.6 ± 0.6</td>
<td>0.70 (0.4743)</td>
<td>0.2</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Preflight, in-flight, and postflight values are means ± SE; $n = 5$ subjects. Only data obtained after intake of placebo are included in the analysis. $F_{2,8}$ represent the $F$ values derived from a 1-factor ANOVA for repeated measures. Paired Student’s $t$-tests were used for pairwise comparisons if the ANOVA was significant. Significant differences: *in flight vs. postflight, $P < 0.05$; †in flight vs. postflight, $P < 0.01$; ‡in flight vs. preflight, $P < 0.05$; §in flight vs. preflight, $P < 0.01$.

**Fig. 3.** Self-assessment of sleep quality ($n = 5$). A: subjective sleep quality as assessed on awakening during the preflight segment (L-60, L-30, L-7), in flight, and postflight. B: comparison of subjective sleep quality in the first (early flight) and second half (late flight) of the mission. Data after both placebo and melatonin administration are included. Vertical bars indicate ±1 SE.
Polysomnographically Recorded Sleep

Effect of spaceflight. Parameters obtained from polysomnographically recorded sleep exhibited changes across the three global segments of the experiment (Table 1). ANOVA for repeated measures yielded overall trends for slow-wave sleep (SWS) and REM sleep. Pairwise comparisons indicated that in-flight sleep was similar compared with preflight sleep for all parameters. Postflight latency to sleep onset was shorter than in flight. Postflight SWS was reduced compared with preflight SWS, and REM sleep was markedly increased. Furthermore, postflight latency to REM sleep was significantly reduced compared with both in-flight and preflight REM latency.

Effect of melatonin. Polysomnographically recorded sleep parameters after melatonin administration were compared with placebo for the preflight segment (L-60 and L-30) and the in-flight segment by a two-factor ANOVA for repeated measures. A significant effect of the factor melatonin was obtained only for latency to sleep onset (Table 2). Pairwise comparisons indicated that during the preflight segment, melatonin reduced sleep latency. For the in-flight segment no significant effects of melatonin were observed for any of the sleep parameters.

Analysis by Third of Sleep Episode

The time course of wakefulness, SWS, and REM sleep during sleep episodes was analyzed separately for preflight, in flight, and postflight. This analysis revealed several changes over the three segments, as reflected in significant effects of segment or third or significant interactions between these factors (Table 4). Wakefulness in the last third of the sleep episode was higher in flight than preflight. Postflight wakefulness in the first third was reduced compared with preflight. Although for all segments the normal decline of SWS in the course of sleep was observed, some changes occurred. In-flight SWS was lower in the last third of the sleep episode compared with both preflight and postflight. The nocturnal polarity of REM sleep, i.e., increase in the course of sleep, was observed for all segments. Postflight REM sleep was elevated during the first and second third of the sleep episode compared with the corresponding thirds of preflight sleep episodes.

Time Course of Recovery of Sleep After Return to Earth

To further describe the changes in sleep and in particular the time course of recovery from spaceflight, data were analyzed for the early flight, late flight, and the three postflight recordings separately (Table 5). No significant differences were observed between early and late flight. Compared with the average in-flight values, sleep latencies were shorter during the first and second postflight recordings. The percentage of sleep time in REM sleep was 32% during the first postflight recordings and thereafter returned to in-flight levels. The average latency to REM sleep was only 20.3 min during the first postflight recording and returned to normal values thereafter (see Fig. 4). For the sleep recording during which REM% was elevated, SWS% was somewhat below average flight values (and returned to normal values thereafter).

Actigraphic SPT and TST During PSG Night and Non-PSG Night: In Flight

Comparison of TDT and SPT (Table 1) suggested a difference between actigraphic and PSG estimates of sleep duration. To investigate whether this could be related to the intervention of a PSG recording, we compared actigraphically determined SPT and TST during nights for which PSG recordings were (PSG night) or were not (non-PSG night) scheduled for the in-flight segment (Fig. 5). During PSG nights, SPT was 445.9 ± 3.4 compared with 420 ± 8.1 min for non-PSG nights (P = 0.076). TST for PSG nights was 417.5 ± 6.4 min compared with only 381.6 ± 13.1 min for non-PSG nights (P = 0.0215).

Table 4. Effect of spaceflight on time course of selected PSG parameters

<table>
<thead>
<tr>
<th></th>
<th>Preflight</th>
<th>In Flight</th>
<th>Postflight</th>
<th>F_{4,16} (P = )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wake, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>19.6 ± 4.2</td>
<td>15.2 ± 4.1</td>
<td>11.3 ± 2.9</td>
<td>S_{2,4} = 0.08 (0.8363)</td>
</tr>
<tr>
<td>II</td>
<td>12.0 ± 2.8</td>
<td>8.1 ± 0.7</td>
<td>16.9 ± 6.2</td>
<td>T_{2,4} = 3.49 (0.1249)</td>
</tr>
<tr>
<td>III</td>
<td>17.1 ± 3.2</td>
<td>24.7 ± 4.3</td>
<td>18.2 ± 3.3</td>
<td>S X T_{4,16} = 3.00 (0.0506)</td>
</tr>
<tr>
<td>SWS, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>28.0 ± 4.7</td>
<td>31.4 ± 5.2</td>
<td>21.9 ± 2.1</td>
<td>S_{2,4} = 3.13 (0.0993)</td>
</tr>
<tr>
<td>II</td>
<td>12.2 ± 0.8</td>
<td>6.9 ± 3.5</td>
<td>2.8 ± 1.3</td>
<td>S_{2,4} = 47.87 (0.0001)</td>
</tr>
<tr>
<td>III</td>
<td>3.5 ± 1.0</td>
<td>0.6 ± 0.3</td>
<td>3.3 ± 0.9</td>
<td>S X T_{4,16} = 2.75 (0.0649)</td>
</tr>
<tr>
<td>REM, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>14.6 ± 2.7</td>
<td>16.3 ± 2.3</td>
<td>20.2 ± 2.0</td>
<td>S_{2,4} = 2.98 (0.1388)</td>
</tr>
<tr>
<td>II</td>
<td>25.6 ± 3.4</td>
<td>25.7 ± 3.6</td>
<td>33.0 ± 2.0</td>
<td>T_{2,4} = 38.07 (0.0001)</td>
</tr>
<tr>
<td>III</td>
<td>32.5 ± 3.1</td>
<td>26.1 ± 3.0</td>
<td>34.2 ± 2.2</td>
<td>S X T_{4,16} = 1.23 (0.3389)</td>
</tr>
</tbody>
</table>

Preflight, in-flight, and postflight values are means ± SE; n = 5 subjects. I, II, and III refer to first, second, and final third of sleep episode. SWS, slow-wave sleep. S_{2,4}, effect of factor segment (preflight, in flight, postflight); T_{2,4}, effect of factor third of sleep episode (I–III); S X T_{4,16}, interaction of factor third of sleep episode and segment. *P < 0.05, **P < 0.1, in flight vs. preflight; †P < 0.05, ‡P < 0.01, postflight vs. preflight; ($)P < 0.1, in flight vs. postflight.
To identify whether the short SPTs during flight were related to delayed bedtime or advanced wake time, the intervals between scheduled bed time and actual beginning of the sleep episode as well as the interval between scheduled wake time and actual end of the sleep episode were computed for the Neurolab subjects \( n = 4 \). Figure 6A illustrates the timing of sleep onset and sleep offset in the course of the Neurolab mission. Averaged over all sleep episodes, the interval between scheduled beginning and actual beginning of the sleep episode was 47.6 ± 4.6 min. The interval between actual end and scheduled end was 7.7 ± 2.6 min. Computed separately for the non-PSG and PSG nights, the delay at the beginning of the sleep episode was 55.3 ± 6.3 and 24.6 ± 3.4 min for the non-PSG and PSG nights, respectively. At the end of the sleep episodes, the intervals were 7.9 ± 3.8 and 7.4 ± 2.0 min for the non-PSG and PSG nights, respectively. After inclusion of the STS-95 data, the interval between scheduled and actual beginning of the sleep episode was 35.1 ± 13.0 min \( n = 5 \), and the interval between actual end and scheduled end was 17.2 ± 9.6 min \( n = 5 \). Computed separately for the non-PSG and PSG nights, the delay at the beginning of the sleep

### Table 5. PSG sleep parameters during early flight, late flight, and postflight recordings

<table>
<thead>
<tr>
<th></th>
<th>Early Flight</th>
<th>Late Flight</th>
<th>Postflight-1</th>
<th>Postflight-2</th>
<th>Postflight-3</th>
<th>( F_{4,16} (P -) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep latency, min</td>
<td>12.6 ± 2.0</td>
<td>9.5 ± 3.1</td>
<td>5.3 ± 1.6</td>
<td>4.2 ± 0.4</td>
<td>7.3 ± 2.6</td>
<td>3.07(0.0969)</td>
</tr>
<tr>
<td>TST, min</td>
<td>371.7 ± 15.7</td>
<td>410.6 ± 22.3</td>
<td>438.3 ± 26.5</td>
<td>397.2 ± 19.5</td>
<td>379.8 ± 23.7</td>
<td>2.09(0.1300)</td>
</tr>
<tr>
<td>Sleep efficiency, %</td>
<td>80.9 ± 4.4</td>
<td>87.1 ± 3.7</td>
<td>87.5 ± 3.2</td>
<td>84.8 ± 3.8</td>
<td>81.4 ± 5.4</td>
<td>1.05(0.4109)</td>
</tr>
<tr>
<td>Stage 1, %</td>
<td>16.1 ± 3.6</td>
<td>10.5 ± 0.8</td>
<td>15.9 ± 4.3</td>
<td>19.9 ± 3.1</td>
<td>16.3 ± 2.1</td>
<td>1.77(0.1837)</td>
</tr>
<tr>
<td>Stage 2, %</td>
<td>48.0 ± 2.4</td>
<td>52.2 ± 2.5</td>
<td>43.6 ± 2.8</td>
<td>46.3 ± 1.6</td>
<td>40.9 ± 3.8</td>
<td>2.98(0.0923)</td>
</tr>
<tr>
<td>SWS, %</td>
<td>14.2 ± 4.1</td>
<td>13.3 ± 2.1</td>
<td>8.3 ± 2.2</td>
<td>6.5 ± 1.6</td>
<td>15.2 ± 1.6</td>
<td>2.37(0.1017)</td>
</tr>
<tr>
<td>REM, %</td>
<td>21.7 ± 3.5</td>
<td>24.0 ± 2.6</td>
<td>32.2 ± 2.6</td>
<td>27.4 ± 2.8</td>
<td>27.6 ± 1.5</td>
<td>2.25(0.1155)</td>
</tr>
<tr>
<td>REM latency, min</td>
<td>69.1 ± 4.7</td>
<td>79.5 ± 4.7</td>
<td>20.3 ± 8.4*</td>
<td>48.9 ± 10.4</td>
<td>60.6 ± 7.3</td>
<td>8.22(0.0024)</td>
</tr>
</tbody>
</table>

Values are means ± SE; \( n = 5 \). Only data obtained after intake of placebo are included in the analysis. Postflight-1, -2, and -3 refer to postflight nights 2, 4, and 5, respectively. \( F_{4,16} \) represents the \( F \) values for the factor segment (early flight, late flight, postflight-1, -2, and -3) derived from a repeated-measures ANOVA. Paired \( t \)-tests were used for pairwise comparisons in case the ANOVA was significant. Significant difference: *Postflight (-1, -2, or -3) vs. in-flight average, \( P < 0.01 \).
the mood measures, significant effects of melatonin were observed for 5 of 16 VAS items, with subjects reporting feeling less “competent” after melatonin administration preflight, and less “attentive,” more “sad,” more “sociable,” and less “quick-witted” after melatonin administration in flight. On the KSS, subjects reported greater sleepiness after melatonin administration in flight.

Effect of spaceflight. The effect of spaceflight was examined by comparing combined melatonin and placebo data across preflight, in-flight, and postflight segments for all neurobehavioral performance and mood variables using a one-factor repeated-measures ANOVA. Several mood measures varied over the three segments (see Table 6). On the VAS, subjects reported feeling more “friendly” and “sociable” in flight compared with preflight. They also reported feeling more “energetic,” more “relaxed,” and more “well-coordinated” postflight compared with in flight. Subjects’ self-evaluated performance differed significantly across segments, with performance on the battery rated as best postflight and worst in flight. Other performance and mood variables (e.g., PVT, PRM, and KSS) exhibited a consistent trend toward poorest performance (e.g., most lapses, fewest words recalled, greatest sleepiness, and most effort expended) in flight compared with preflight and postflight. A detailed analysis of the time course of changes in neurobehavioral measures suggested that many of them exhibited a decline during the L-7 segment, a further decline in flight, and a slow recovery postflight. This time course is illustrated for two measures derived from the PVT and two measures derived from the PRM in Fig. 7.

PVT lapses and the number of words correctly recalled on the PRM task show evidence of poorer performance during the preflight-7 session just before launch, with a continuation of poorer performance during flight and an improvement postflight. This was in part confirmed by ANOVA, which yielded a near significant effect for the factor segment (with 8 levels) for number of lapses on the PVT ($F_{7,31} = 2.31; P < 0.0516$) but not for the median reaction time ($F_{7,31} = 0.61; P < 0.7423$). Likewise, ANOVA yielded a significant effect for the factor segment (with 8 levels) for number of words recalled ($F_{7,31} = 2.78; P < 0.0231$) but not for recall time ($F_{7,31} = 0.94; P < 0.4936$).

Illuminance in the Three Habitable Compartments of the Space Shuttle

The temporal patterning and average illuminances were very different in the three habitable compartments of the space shuttle. On the flight deck the two major periodicities that were clearly visible in the raw data were the ~23-h 40-min period associated with scheduled sleep and wakefulness and the ~90-min cycle associated with the orbit of the spacecraft around the earth. In contrast, on the middeck and in the Spacelab, only the ~23-h 40-min period, and some

Neurobehavioral Assessment

Effect of melatonin. Neurobehavioral performance and mood in the afternoon after nighttime melatonin administration were compared with placebo for the preflight segment (L-60 and L-30) and the in-flight segment by a two-factor ANOVA for repeated measures. There were no significant effects of melatonin for any of the neurobehavioral performance measures. For episode was $42.1 \pm 14.1$ min ($n = 5$) and $15.9 \pm 9.2$ min ($n = 5$) for the non-PSG and PSG nights, respectively. At the end of the sleep episodes, the intervals were $16.1 \pm 8.8$ min ($n = 5$) and $18.0 \pm 10.7$ ($n = 5$) for the non-PSG and PSG nights, respectively. These values were also computed separately for the placebo and melatonin administrations. There were no significant effects of melatonin for the mood measures, significant effects of melatonin were observed for 5 of 16 VAS items, with subjects reporting feeling less “competent” after melatonin administration preflight, and less “attentive,” more “sad,” more “sociable,” and less “quick-witted” after melatonin administration in flight. On the KSS, subjects reported greater sleepiness after melatonin administration in flight. To assess effects of flight on neurobehavioral and mood measures, melatonin and placebo data were combined.

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deviations from this schedule, could be detected. A detailed plot (Fig. 8, left) of a 48-h segment of the data from STS-90 illustrates the wide range of illuminances present on the flight deck, as well as the high values observed during each orbital dawn. Orbital dawns can even be observed during scheduled sleep episodes when the windows on the flight deck were covered with shades. The average, minimum, and maximum illuminance was computed separately for the three compartments and separately for the scheduled sleep and wake episodes, as well as separately for STS-90 and STS-95. The frequency distribution of illuminances was computed separately for scheduled sleep and scheduled wakefulness for the three compartments during the Neurolab mission (Fig. 8, right). The average illumination (both arithmetic and geometric means) was highest on the flight deck and lowest on the middeck (Table 7). Variability was considerable on the flight deck and minimal in the Spacelab and on the middeck. Thus the highest value observed on the flight deck was close to 80,000 lx, whereas on the middeck and in the Spacelab these values were 93 and 171 lx, respectively. The frequency distributions plotted in Fig. 8 illustrate the highly variable light environment on the flight deck, especially during scheduled wakefulness and the very low and relatively stable levels on the middeck in particular. The presence of illuminance levels in the 1- to 10-lx range in the Spacelab during scheduled sleep episodes (Fig. 8, bottom right) was related to scheduled sleep episodes during which lights were not turned off.

For STS-95 similar illuminance values were observed although values on the middeck and in the Spacehab were slightly higher.

**Time course of illuminance at the transition of scheduled sleep and scheduled wake episodes.** The time course of illuminance at the transitions from scheduled wake to scheduled sleep and vice versa was analyzed for the STS-90 mission for the flight deck and middeck separately (Fig. 9). At the scheduled transition from sleep to wakefulness, illuminance increased promptly and rapidly on both the flight deck and middeck. In
contrast, at the scheduled time for the transition from wakefulness to sleep, it took 40–80 min before illumination reached low values. The gradual reduction of light exposure after scheduled lights out may be a consequence of averaging days with sharp light/dark transitions each but occurring at different times after scheduled lights out.

Body Temperature

Acceptable temperature data were obtained during the L-60 segment as well as during the early and late flight segments (Fig. 10). The time course of temperature during preflight was characterized by rapid increases and decreases of temperature at the transition from and to sleep. During early flight and in particular during late flight, temperature appeared to rise more gradually during the waking episode. Before flight, average temperature was 37.16 ± 0.4 and 36.55 ± 0.7°C (SE) for wake and sleep episodes, respectively. During early flight these values were 37.05 ± 0.10 and 36.61 ± 0.016°C, respectively. During late flight, temperature in the wake episode remained comparable (37.05 ± 0.09°C), but temperature in the sleep episode (36.72 ± 0.7°C) was somewhat higher than during preflight and early in flight. Quantification of the circadian waveform of body temperature revealed an amplitude of 0.43 ± 0.01 (SE) (95% CI 0.40–0.45), 0.37 ± 0.01 (95% CI 0.35–0.39), and 0.24 ± 0.01 (95% CI 0.22–0.27)°C for the L-60, early flight, and late flight, respectively. The 95% CI of these estimated did not overlap. This indicates a significant reduction in the amplitude of the body temperature from L-60 to early flight and from early flight to late flight. During all three segments the minimum of the curve fitted to average temperature curves was located within the sleep episodes even though during late flight the end of the scheduled sleep episode occurred 3.1 h earlier than during early flight.

Cortisol

In the Neurolab astronauts, urinary cortisol excretion averaged 0.47 ± 0.08 (SE) (n = 4) preflight, 0.57 ± 0.10 during early flight, 0.55 ± 0.12 during late flight, and 0.49 ± 0.05 μg/min postflight. Although urinary cortisol excretion appeared higher during flight, neither pairwise comparisons nor ANOVA indicated that this change was statistically significant. The average cortisol secretion data, derived from urinary measures, indicated no obvious change in the phase relationship between the scheduled sleep-wake cycle and the urinary cortisol rhythm during early flight. However, during late flight the falling limb of the cortisol rhythm appeared delayed relative to the scheduled sleep episode. Postflight the normal phase relationship between the urinary cortisol rhythm and scheduled sleep was reestablished (Fig. 11).

DISCUSSION

Working and sleeping in space, while living on shorter than 24-h rest-activity cycles and being exposed to highly variable and complex light-dark cycles, was associated in these crewmembers with an apparent reduction in subjective sleep quality and actigraphically recorded sleep period time, decrements in neurobehavioral performance, and a delay of the circadian rhythm of cortisol relative to the scheduled sleep-wake cycle. PSG recording of sleep was associated with an increase in sleep duration compared with sleep durations on nights when the PSG sleep recordings were not part of the crew’s duty assignment. On return to Earth a marked increase in REM sleep occurred, and subjective sleep quality and neurobehavioral performance recovered.

Sleep reduction associated with spaceflight has been reported repeatedly (15, 16, 18–20, 22, 30, 36), and the average duration of sleep was 6–6.5 h in all of these reports. Our current estimate of sleep duration derived from actigraphy and sleep logs is in good accordance...
with these reports. Previously it was demonstrated that also during spaceflight, estimates of sleep duration as derived from actigraphy correlate well with concurrently obtained PSG estimates (31). It thus appears that sleep loss is a strongly reproducible finding and a salient aspect of living in space for ~2 wk. During the sleep episodes that were recorded polysomnographically, sleep duration was significantly longer than on the other nights. Our interpretation, based on the analysis of the timing of the onset and offset of sleep relative to the scheduled timing of these events on PSG and non-PSG nights, is that astronauts were very motivated to participate in the sleep experiment and adhered more closely to scheduled bedtimes on these PSG nights. During non-PSG nights, when sleep was recorded through actigraphy, sleep duration was shorter. This would imply that during spaceflights during which astronauts are not participating in sleep experiments, sleep is more disrupted than reported here for the PSG nights.

The results from the PSG recordings obtained during spaceflight demonstrate that sleep structure and sleep efficiency were comparable to preflight baseline. A reduction of SWS was only observed in the last third of sleep episodes in space. This effect is smaller in magnitude than the reduction of SWS during a similar mission (30). On return from space, sleep latency and REM latency were very short, and the percentage of REM sleep was markedly elevated in particular during the first sleep recording (second sleep episode on return). Changes in REM sleep have been reported for Mir missions (22) and Skylab missions (15, 16). In the present experiment, the increase of REM sleep on return from space may either represent a response specific to spaceflight or, alternatively, may be a consequence of the abrupt delay of the sleep episode relative to the timing of sleep in space. Such a delay of the sleep-wake cycle could result in sleep on return being scheduled later in the circadian cycle, i.e., closer to the crest of the REM sleep propensity rhythm (9). However, the urinary cortisol data indicate that sleep on return occurred at a circadian phase similar to preflight, suggesting that minimal circadian adaptation to the imposed sleep-wake schedule occurred during spaceflight. Thus the short REM and sleep latencies as well as the high percentage of REM sleep and the somewhat reduced percentage of SWS observed on return may represent a genuine consequence of spaceflight and the subsequent readaptation to the 1-G environment. These considerations highlight the importance of accurate circadian phase assessments for the interpretation of sleep data collected during and after spaceflight.

Fig. 8. Left: time course of illuminance (48-h segment) recorded on the flight deck (top), middeck (middle), and in the Spacelab (bottom). Right: relative frequency distribution of illuminances (bin width 0.5 log units) during scheduled wakefulness (heavy solid line) and scheduled sleep (thin solid line) for the flight deck (top), middeck (middle), and Spacelab (bottom). Frequency distributions were derived from all data collected during the STS-90 mission.
spaceflight. To investigate whether spaceflight and subsequent return to 1 G are associated with specific activation of REM sleep-regulatory processes, sleep during and after spaceflight should be scheduled to nearly identical circadian phases. This requirement was not met in the present and most previous studies, although Frost et al. (15) have argued that the (delayed) postflight REM increase observed after long-duration Skylab missions was unlikely to be due to circadian rhythm changes. Establishing that spaceflight per se is associated with an increase in REM sleep on return to Earth and the associated readaptation to gravity could be a promising avenue for future research on the effects of spaceflight on sleep regulation.

Putative Causes of the Reduction in TST During Spaceflight

Reduced TST appears a robust finding in studies on sleep in space. Furthermore, the frequent use of hypnotics (33) and the subjective estimates of sleep quality and duration (36) reported previously in conjunction with our current data indicate that sleep is disturbed. In particular, it appears that the subjectively perceived recuperative quality of sleep is significantly reduced during spaceflight, this despite the observation that objective parameters of sleep efficiency and sleep structure do not indicate major abnormalities. Our analyses of respiration during these sleep episodes have demonstrated that sleep-related respiratory disturbances are reduced during spaceflight. Thus respiratory disturbances can be excluded as a cause of the reduced sleep quality (14). The causes of this reduction in sleep duration and quality could be manifold. Our analyses of the time course of illuminance and analyses based on actigraphy data from STS-90 demonstrate that the onset of sleep episodes in particular is delayed. This is very similar to the recent analysis of the relationship between time in bed and bedtime during a 438-day Mir mission (19). The reasons for this delay of bedtime could be operational demands or social and recreational activities. It appears that control of the lights was exerted primarily by the orbiter crew. We should not dismiss a role of the circadian timing system in the facilitation of voluntary decisions to end the waking day: if in the current studies scheduled sleep time was advanced with respect to the opening of the sleep gate, the circadian timing system, i.e., the strong drive for wakefulness present shortly before habitual bedtime, in combination with operational demands and opportunities to enjoy more views of Earth, could easily result in a tendency to delay the turning off of the lights. Because such an opportunity to delay the transition between vigilance states is not present at the

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<th>Table 7. Illuminance on the flight deck, middeck, and in the Spacelab (STS-90)/Spacehab (STS-95)</th>
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Values are illuminances in lx. Illuminance during wake and sleep are observed illuminances during scheduled wake and sleep episodes. Means are based on continuous measurements throughout the missions.

Fig. 9. Time course of illuminance on the flight deck (●) and middeck (○) relative to scheduled bedtime [i.e., scheduled lights out (A)] and scheduled wake time [i.e., scheduled lights on (B)]. Vertical lines indicate the time of scheduled lights out (A) and lights on (B). Data represent arithmetic means of all mission days during STS-90.
other end of the sleep episode (i.e., the reveille will be on time), total time for sleep is reduced.

**Melatonin**

During spaceflight direct beneficial effects of 0.3 mg of melatonin on sleep were not observed. Determination of 6-sulfatoxymelatonin concentration in available urine samples collected in the morning after scheduled intake of melatonin or placebo indicated that melatonin capsules had been taken according to administration schedule. The average timing of the sleep episodes as derived from actigraphy is indicated by the open vertical boxes. Average temperature is indicated by the heavy solid line. Thin lines indicate +1 SE and −1 SE.

controlled laboratory conditions, and this effect, even though random, could have reduced our ability to detect an effect of melatonin. Alternatively, this lack of efficacy may be related to insufficient desynchrony between the scheduled sleep-wake cycle and endogenous circadian rhythmicity. Available data indicate that exogenous melatonin can increase total sleep time and sleep efficiency when sleep is scheduled during the

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**Fig. 10.** Core body temperature of astronauts (n = 4, Neurolab) −2 mo before launch (L-60; A), during early flight (B), and during late flight (C). The average timing of the sleep episodes as derived from actigraphy is indicated by the open vertical boxes. Average temperature is indicated by the heavy solid line. Thin lines indicate +1 SE and −1 SE.

**Fig. 11.** Urinary cortisol excretion of Neurolab astronauts (n = 4) during the preflight segment (A), early flight (B), late flight (C), and postflight (D). Data are aligned with respect to the scheduled beginning of the 1st sleep episode in each 32-h segment. The preflight data from A are replotted (thin line) in B–D for purposes of comparison. Thick solid lines in B–D represent the data obtained during these respective segments. The preflight segment represents the average of L-60, L-30, and L-7 segments, which results in an apparent higher temporal resolution of this time series.
The observed effects of spaceflight on sleep were virtually identical when the data were pooled.

**Neurobehavioral Parameters**

The time course of neurobehavioral performance, and in particular the recovery on return, indicated that neurobehavioral performance is adversely affected during spaceflight. This conclusion is strengthened by the observation that many indexes of performance followed a nearly identical time course. Although previous studies have reported negative effects of spaceflight on performance, such effects were often limited to specific tasks such as tracking tasks (28). Whether the changes in neurobehavioral measures that were observed in the present study are related to sleep loss, workload, stress, and sleep deprivation, already exerts a negative impact on performance. Preflight work and sleep schedules may have to be reconsidered to prevent this.

**Illuminance and Circadian Parameters**

The temporal patterns of illuminance were remarkably variable between the three habitable compartments. The complex light-dark cycles on the flight deck, with very high maximum levels, contrasted with the very low and nearly constant levels in the Spacelab and middeck. The higher and more variable levels in the Spacehab (STS-95) are probably related to the portholes present in this compartment.

Because astronauts move between the three compartments, the consequences of these different light environments for light-exposure remain unclear. The payload and mission specialists involved in scientific experiments will, however, spend most of their working day in either the Spacelab or middeck. Consequently, they will not be exposed to high light levels. This is in accordance with the data by Monk and colleagues (30), who reported that four astronauts on STS-78 were on average exposed to 70 lx in flight. It is, however, unclear whether this latter value represents a mean over the 24-h period or the wake period. Nevertheless, it appears that during STS-90 illuminance was even lower than during STS-78.

The waveform of body temperature when aligned with the onset of the sleep episode indicated that even in microgravity, sleep episodes are associated with an evoked temperature-lowering effect. These effects may be associated with changes in activity levels. We have previously shown that such masked temperature data do not accurately reflect the circadian phase of this rhythm (10, 25), and therefore these data cannot be taken as evidence that the circadian system remained synchronized to the shorter than 24-h rest-activity cycle. The waveform of the temperature cycle and the fitted amplitude changed during spaceflight. The sawtooth waveform observed in the later part of the flight and the reduced amplitude again are in accordance with the data obtained during STS-78 (30) in astronauts and in monkeys by Fuller and colleagues (17). It should be noted that reductions in amplitude were also observed during a bedrest study (29) and thus may be associated with the absence of changes in posture in the microgravity environment. However, during the STS-90 mission, the amplitude of the fitted fundamental to the body temperature data became progressively smaller from L-60 to early flight to late flight. Such a progressive change in the amplitude in the course of the mission is difficult to explain by an absence of changes in posture. This reduction in the amplitude could indicate a change in the phase relationship between the endogenous circadian component of the body temperature rhythm and the evoked components. The observed changes in the waveform could also be related to a change in the phase relationship between the endogenous and the evoked component. Alternatively, these changes in amplitude and waveform may reflect dissociation between the circadian phases of individual astronauts.

The urinary cortisol data indicated that endogenous circadian rhythms failed to advance at the same rate as the shorter than 24-h sleep-wake cycle. Although the estimates of the cortisol rhythm were only derived from urine samples, which have an inherently low temporal resolution, these data and the observed changes in the waveform of the body temperature rhythm imply that the light exposure and the scheduling of the sleep-wake cycle itself exerted insufficient drive onto the pacemaker to maintain synchrony. These data are in accordance with the 2-h phase delay of body temperature rhythm reported during a Mir mission (22) but are at variance with the interpretation of the data on circadian phase derived from temperature, cortisol, and melatonin obtained during STS-78. During this mission the sleep-wake schedule was nearly identical (i.e., an advance of 25 min/day) to the current missions (20 and 35 min/day for the STS-90 and STS-95 missions, respectively). This discrepancy between these studies may be related to the lower light levels during the STS-90 mission compared with STS-78. In previous studies on the effects of spaceflight on cortisol secretion, some indication for an increase of secretion has been obtained (38). Although statistical analysis of our data did not reveal significant increases, a trend toward higher cortisol levels in flight was observed.

More accurate assessments of circadian phase during future space missions are required to assess conclusively whether circadian misalignment occurs. Nevertheless, the present data show circadian abnormalities, i.e., reduced amplitude and altered waveform of the body temperature rhythm and an apparent delay in the rhythm of cortisol during spaceflight.
Conclusion

The current data and analyses underscore the manifold changes that occur during spaceflight. Some of these changes were quantified by simple noninvasive continuous actigraphic assessment of rest-activity cycles and assessment of subjective sleep quality with simple questionnaires. Neurobeh-avioral, physiological, endocrinological, and polysomnographic assessments revealed changes in neurobehavioral performance, endocrine rhythms, and temperature physiology, as well as changes in REM sleep regulation. Causes of these changes could be varied. In this study we quantified the abnormal light-dark cycle, which, in view of its variability and low intensity, could be a contributing factor to circadian misalignment. Detailed analyses of the rest-activity cycles revealed that sleep reduction may occur because of delayed initiation of the sleep episodes. Other changes, such as the prominent increase in REM sleep on return to Earth, remain to be explained. Likewise, it remains to be elucidated whether the observed decrements in neurobehavioral performance are related to sleep loss, the circadian misalignment, or to other factors associated with spaceflight. Nevertheless, these data demonstrate that changes in these variables occur and imply that successful adaptation to an environment different from the environment in which regulatory mechanisms for sleep and circadian rhythms evolved remains challenging.

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